Dermatology beyond the skin

Cover Page

Official title: A phase 3 trial comparing the efficacy and safety of LEO 90100 aerosol foam with the aerosol foam vehicle used twice weekly as long-term maintenance therapy in subjects with psoriasis vulgaris.
LEO Pharma number: LP0053-1004
NCT number: NCT02899962
Date: 15-Jul-2019

Statistical Analysis Plan

LEO 90100 twice weekly maintenance regimen for psoriasis vulgaris

A phase 3 trial comparing the efficacy and safety of LEO 90100 aerosol foam with the aerosol foam vehicle used twice weekly as long-term maintenance therapy in subjects with psoriasis vulgaris.

A 12-month, international, multi-centre, randomised, vehicle controlled, double-blind, 2-arm, parallel group trial.

LEO Pharma A/S	**Trial ID:**	**LP0053-1004**
	Date:	**15-JUL-2019**
	Version:	**1.0**

1 Statistical Analysis Plan Approval

1.1 Approval Statement

On behalf of LEO, the Biostatistics Lead and the Medical Lead, are authorised to approve the Statistical Analysis Plan Update.

The QC statistician has by approving this document confirmed that the statistical information has been subject to statistical quality control.

The following persons have approved this Statistical Analysis Plan Update using electronic signatures as presented on the last page of this document.

PPD

Biostatistics Lead, Global Clinical Operations

PPD

Medical Lead, Medical Science

PPD

QC Statistician, Biostatistics

2 Statistical Analysis Plan Statements

2.1 Compliance with Good Clinical Practice

This Statistical Analysis Plan Update is designed to comply with the standards issued by the International Conference on Harmonisation (ICH) (E3: Structure and Content of Clinical Study Reports, E6: Good Clinical Practice, and E9: Statistical Principles for Clinical Trials).

Table of Contents

3 List of Abbreviations

ACTH	Adrenocorticotropic Hormone
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
BSA	Body Surface Area
CPM	Clinical Project Manager
CPMP	Committee for Proprietary Medicinal Products
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organisation
DK	Denmark
DLQI	Dermatology Life Quality Index
eCRF	Electronic Case Report Form
eDiary	Electronic Diary
EU	European Union
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IMP	Investigational Product
IRB	Institutional Review Board
m-PASI	Modified Psoriasis Area Severity Index
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed effect Model Repeat Measurement
ML	Maximum Likelihood
PASI	Psoriasis Area Severity Index
PASI 75	A 75% reduction in the modified Psoriasis Area Severity Index
PGA	Physician's Global Assessment of Disease Severity
PRO	Patient Reported Outcome
PSI	Psoriasis Symptom Inventory
REML	Restricted Maximum Likelihood
SAE	Serious Adverse Event

SAP	Statistical Analysis Plan
SD	Standard Deviation
SGA	Subject's global assessment of disease severity
SOC	System Organ Class
SOP	Standard Operating Procedure
UNS	Unscheduled Visit

4 Introduction

The statistical analysis will be performed as outlined in the Clinical Trial Protocol including amendments. This statistical analysis plan, prepared before the unblinding of the trial, but after the blind review of the data, contains a more technical and detailed elaboration of some points in the statistical analysis described in the Clinical Trial Protocol. Deviations from the planned data presentation and analysis are also described in section 5.7. Furthermore, the analysis sets, which are to be used for the statistical analysis, are presented.

5 Statistical Analysis

5.1 Definition of trial periods

The trial periods are defined in Table 1.

Table 1: Definition of trial periods

Trial period	Definition
Open-label phase	From the day of enrolment to the day before randomisation.
Randomised phase	From the day of randomisation to end of trial, both days included.
Maintenance phase	From the day of first exposure to maintenance IMP to the last day of exposure (rescue or maintenance IMP), both days included.
Follow-up phase	From the day after last application of maintenance or rescue IMP to end of trial.
Relapse period	Relapse is defined as a PGA score of at least 'mild' during the maintenance phase, for details on relapse see CTP section 6.14.1. A relapse period is defined from the relapse start day (included) to the

	visit date when relapse treatment is discontinued (not included).
Remission period	A remission period is a period where the subject is not in a relapse period within the maintenance phase.
Visit interval	The interval between two successive scheduled visits.

5.2 Trial Analysis Sets

The trial analysis sets are defined in Table 2. The analysis sets are described in more detail in the Analysis Set Definition Document.

Table 2: Trial analysis sets

Analysis set	**Definition**
Enrolled subjects	All subjects enrolled (informed consent obtained) in the trial.
Open-label safety analysis set	All subjects exposed to LEO 90100 during the open-label phase.
Open-label HPA analysis set	All subjects in the open-label safety analysis set who provided consent for the Adrenocorticotropic Hormone (ACTH) challenge test and underwent a Hypothalamic-Pituitary-Adrenal (HPA) axis test.
Full analysis set	All subjects randomised who had treatment success at randomisation, defined as PGA score of 'clear' or 'almost clear' with at least a 2-grade improvement from baseline. Subjects randomised without treatment success will be excluded from the full analysis set. This approach is in alignment with the ICH E9, since achieving treatment success is a major randomisation criterion measured prior to randomisation and therefore exclusion of such subjects will not introduce bias.
Per protocol analysis set	The per protocol analysis set will be defined by excluding subjects from the full analysis set as described in the protocol and in the Analysis Set Definition Document.
Safety analysis	All subjects exposed to IMPs following randomisation and with available

set	post-randomisation safety evaluations.
Randomised subjects	All subjects randomised to the maintenance phase.
HPA analysis set	All subjects in the safety analysis set who provided consent for the ACTH challenge test and underwent an HPA axis test.

5.3 Baseline Considerations

5.3.1 Baseline definition

As described in the protocol, baseline is defined as the measurement taken at screening or visit 1.
The maintenance phase baseline is defined as the last available measurement collected at randomisation (visit 2).

Baseline for rebounds will be handled differently as described in section 5.5.4.

5.3.2 Disposition of subjects

The reason for leaving the trial will be presented as described in the protocol.

In addition, cumulative incidence plots of discontinuation by reason for withdrawal will be done for subjects leaving the trial during the open-label phase or the maintenance phase, respectively. The plots for the maintenance phase will be presented by treatment group.

Further details for the tables can be found in Appendix I and Appendix II.

5.3.3 Demographics

Demographics and other baseline characteristics will be presented as described in the protocol. Age groups (18-64, >=65) will also be presented for all enrolled subjects and for all randomised subjects by treatment group.

More details for tables for demographics and other baseline characteristics are given in Appendix I and Appendix II.

5.3.4 Compliance

For the open-label treatment phase, number of subjects in non-compliance with treatment instructions together with percentage of missed daily applications of IMP will be summarised for the open-label safety analysis set.

For the maintenance phase, number of subjects in non-compliance with maintenance treatment instructions (i.e.; excluding relapse periods) will be summarised by treatment group both for each visit interval and for the total maintenance phase for the safety analysis set. The compliance information will be assigned to the visit interval by collection date.

For the relapse periods, number of subjects in non-compliance with rescue treatment instructions and percentage of missed daily applications of rescue IMP will be summarised by treatment group for the safety analysis set.

For an overview of changes as compared to the protocol refer to section 5.7.

5.4 Analysis of Efficacy

The assessment of efficacy is done for the maintenance phase. The primary and secondary efficacy endpoints will be analysed for the full analysis set, with the analyses for the per protocol analysis set being supportive. Sensitivity analyses are done for the full analysis set. Trial sites will be pooled as described in section 5.6.4 and will be referred as pooled sites.

5.4.1 Primary Efficacy Endpoint

The primary endpoint will be analysed using a cox proportional hazards model with treatment group, pooled sites, and disease severity at maintenance baseline (as determined by the PGA) as factors. Maintenance baseline is used in the model as compared to baseline at visit 1. See section 5.7 for details regarding changes as compared to the protocol.

The survival curves will be estimated using the Kaplan-Meier estimator. A log-log transformation will be applied to the survival function to obtain the pointwise confidence intervals in addition to the confidence intervals for the percentiles of the estimated survival times. The estimated survival curves and the confidence limits will be shown graphically. The percentiles of the estimated survival distribution and 95% confidence limits for the percentiles will be tabulated by treatment group.

Number of subjects still at risk of first relapse at timepoints for scheduled visits will be summarised by treatment group.

Further details for tables, figures and listings for the primary endpoint are given in Appendix I and Appendix II.

Sensitivity analysis:
In the sensitivity analysis the primary endpoint will be analysed incorporating interval censoring. We will consider three different types of censoring. Subjects who do not encounter a relapse during the trial and subjects who are withdrawn from the trial in the maintenance phase before having a relapse will be right-censored, and the number of days will be treated as a censored observation at the end date of the maintenance phase. Subjects who are confirmed to have a relapse at a scheduled visit are interval censored, and it is assumed that the start of the relapse is between the scheduled visit where the relapse is confirmed and the previous visit where PGA was measured for the subject. For subjects who are confirmed to have a relapse at an unscheduled visit, it is assumed that the relapse starts on the day of this visit. These subjects are assumed to have exact observations. More details are given in Table 3.

The number of subjects without relapse, the number of subjects with relapse confirmed at a scheduled visit, and the number of subjects with relapse confirmed at an unscheduled visit will be summarised by treatment group.

Table 3: Censoring in the sensitivity analysis of primary endpoint

Relapse information	**Censoring type**	**Observation type**	**Lower endpoint**	**Upper endpoint**
No relapse	Right-censored	(x, .], where x is the day the subject completed the trial or withdrew from the trial, and . denotes that this is left missing	x	. (missing)
Relapse confirmed at scheduled visit	Interval censored	(x, y], where x is the day of the previous visit in which PGA was measured, without relapse, and y is the day of the visit, where relapse is confirmed	x	y
Relapse confirmed at unscheduled visit	Exact observation	[x, x], where x is the day of the visit where relapse is confirmed	x	x

In the sensitivity analysis, time to first relapse during the maintenance phase will be analysed using a proportional hazards model with treatment group, pooled sites, and disease severity at maintenance baseline (determined by the PGA) as factors. The model will incorporate interval censoring. The baseline hazard function is assumed to be a piecewise constant function within ten disjoint intervals. The ten intervals split the time axis such that each interval contains approximately equal number of unique boundary values and imputed middle points. The estimate of the hazard ratio of active treatment group relative to vehicle group together with the 95% confidence interval and p-value will be presented.

Furthermore, survival curves will be estimated using a non-parametric maximum likelihood estimator, namely the Turnbull self-consistency algorithm. Standard errors will be computed using multiple imputation with 1000 samples (seed=39506291). A log-log transformation will be applied to the survival function to obtain the pointwise confidence intervals in addition to the confidence intervals for the percentiles of the estimated survival times. The estimated survival curves and the confidence limits will be shown graphically. The percentiles of the estimated survival distribution and 95% confidence limits for the percentiles will be tabulated by treatment group.

This sensitivity analysis was not specified in the protocol. See section 5.7 for details regarding changes as compared to the protocol.

Further details for tables, figures and listings for the sensitivity analysis are given in Appendix I and Appendix II.

5.4.2 Secondary Efficacy Endpoints

Adjustment for multiplicity will be done as described in the protocol. Further details can be found in section 5.6.4.

5.4.2.1 Proportion of days in remission

The endpoint is the proportion of days in remission as compared to the number of days in remission described in the protocol section 11.3.3.5. Analysis and sensitivity analysis are also different as compared to the protocol. See section 5.7 for details regarding changes to the protocol.

The number of days in remission will be calculated as the sum of days where the subject is in remission periods as defined in Table 1. The proportion of days in remission will be calculated

as the number of days in remission divided by the length of the maintenance phase in days. The proportion of days in remission will be summarised by treatment group.

Multiple imputation:

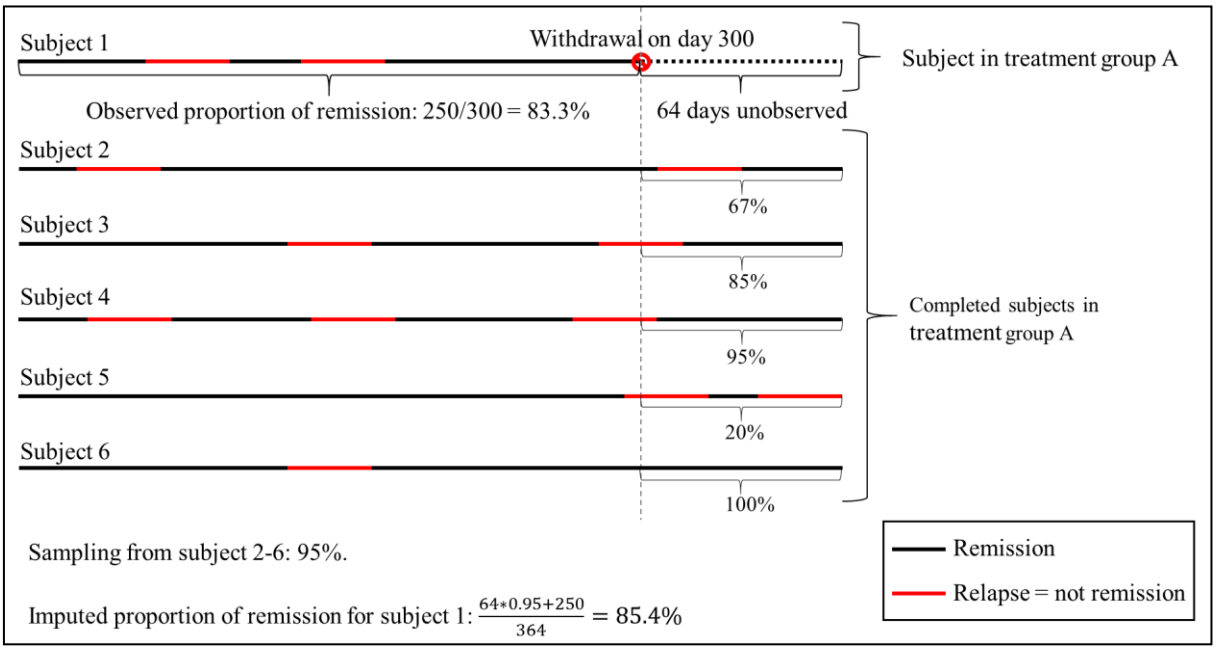
Multiple imputation of data for withdrawn subjects will be done using 100 imputations (seed=20910158). In order not to favour any treatment arm, the imputation approach will depend on whether the subject's reason for withdrawal potentially is related to IMP or not.

For the imputation, the length of the maintenance phase is assumed to be 52 weeks, corresponding to 364 days.

Imputation for subjects withdrawn with reasons 'withdrawal by subject' or 'lost to follow up':

This approach assumes that the unobserved remission pattern for withdrawn subjects will be like the pattern observed for subjects in the same treatment group completing the maintenance phase. An example can be found in Figure 1 and the described below.

Figure 1: Example of imputation for a subject withdrawing from trial due to lost to follow-up or withdrawal by subject



Imputation steps:

1. For a withdrawn subject the 'number of unobserved days' will be computed as 364 minus the length of the subject's maintenance phase. This 'number of unobserved days' (e.g.; 64) will be used in step 2.

2. For the sub-set of subjects, that are in the same treatment group as the withdrawn subject and completed their maintenance phase, the proportion of days in remission will be calculated for the last part in their maintenance phase lasting 'number of days unobserved' (e.g.; 64).

3. A single proportion of days in remission will be randomly sampled from the proportions calculated in step 2. This will be called the 'sampled proportion' (e.g.; 95%)

4. For the withdrawn subject, the number of days in remission for the missing period will be estimated by multiplying the 'sampled proportion' by the 'number of unobserved days' (e.g.; 0.95*64).

5. For the withdrawn subject, the proportion of days in remission will be calculated by summing the observed number of days in remission and the estimated number of days in remission (from step 4) and dividing by 364.

6. Steps 1 to 5 will be repeated 100 times for each withdrawn subject to form 100 complete datasets.

Imputation for subjects withdrawn with reasons 'adverse event', 'death', 'lack of efficacy', or 'subject not achieving clear or almost clear after treatment of relapse':

This approach assumes that the unobserved part of the trial for subjects withdrawn due to these reasons, would have been similar to the observed part of the trial for the subjects withdrawing for the same four reasons regardless of treatment arm. An example can be found in Figure 2 and described in the imputation step below.

Imputation steps:

1. For a withdrawn subject the 'number of unobserved days' (e.g.; 64) will be computed as 364 minus the length of the subject's maintenance phase.

2. For the sub-set of subjects withdrawn due to 'adverse event', 'death', 'lack of efficacy', or 'subject not achieving clear or almost clear after treatment of relapse', the proportion of days in remission will be calculated.

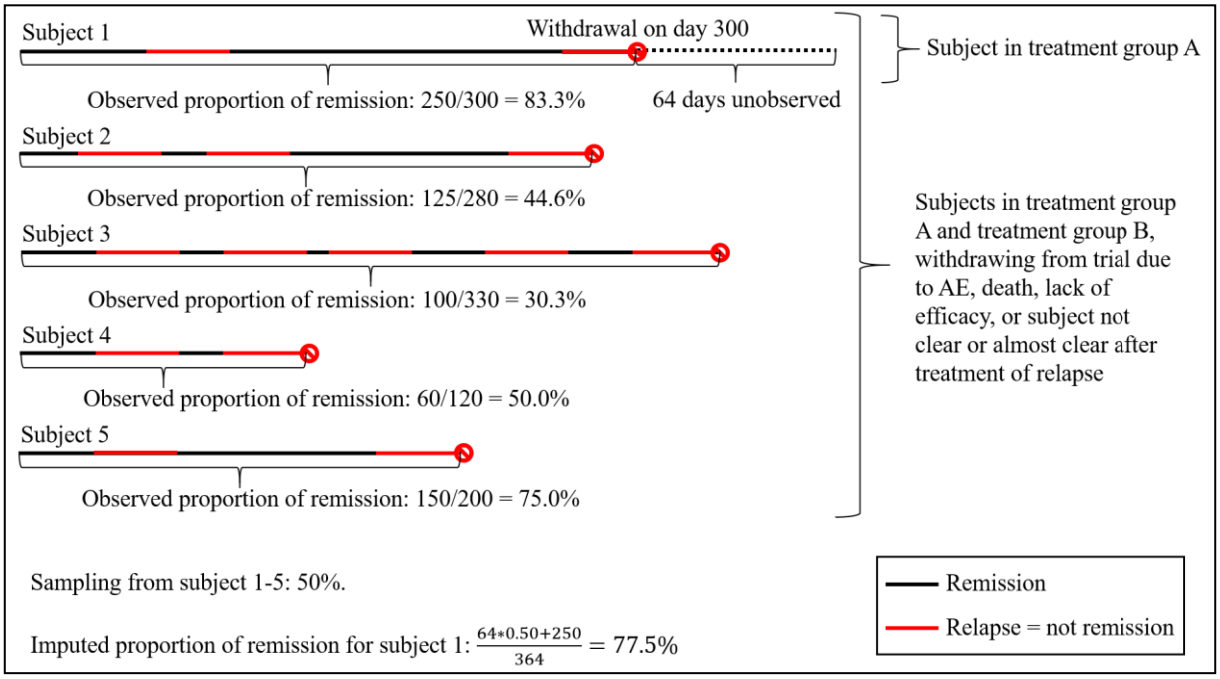
3. A single proportion of days in remission will be randomly sampled from the proportions in step 2. This will be called the 'sampled proportion' (e.g.; 50%)

4. For the withdrawn subject, the number of days in remission for the missing period will be estimated by multiplying the 'sampled proportion' by the 'number of unobserved days' (e.g.; 0.50*64).

5. For the withdrawn subject, the proportion of days in remission will be calculated by summing the observed number of days in remission and the estimated number of days in remission (from step 4) and dividing by 364.

6. Steps 1 to 5 will be repeated 100 times for each withdrawn subject to form 100 complete datasets.

Figure 2: Example of imputation for a subject withdrawing from trial due to AE, death, lack of efficacy, or subject not clear or almost clear after treatment of relapse



Imputation for subjects leaving the trial due to other reasons:

For cases with withdrawal reason specified as 'Other', the details will be revised on a blinded manner, selecting and documenting the imputation approach in the Analysis Set Definition Document.

Statistical analysis:

For each of the 100 complete data sets, the difference in proportion of days in remission between treatment groups will be analysed by means of an analysis of variance (ANOVA) model as described in the protocol section 11.3.3.5. The estimates and standard errors from

the 100 analyses will be pooled to one estimated treatment difference and associated standard error using Rubin's rule to draw inference. From these pooled estimates, the 95% CI for the treatment difference will be calculated. The p-value for treatment difference will be calculated using a two-tailed Student's t-test based on the pooled estimates.

A histogram with a density curve of proportion of days in remission by treatment group will be presented.

Number of days in remission between relapses will be plotted by treatment group.

Sensitivity analysis:
An additional sensitivity analysis will be performed assuming that after the subjects withdrew the pattern of remission will be as if the subject was not treated. This will be done as described above, however in step 2 of the sub-set of subjects will be subjects treated with vehicle.

Further details for tables, figures and listings are given in Appendix I and Appendix II.

5.4.2.2 Number of relapses during maintenance phase

The number of relapses will be analysed using a Poisson regression model with treatment group, pooled sites, and disease severity at maintenance baseline as factors, subject as random effect, and time at risk as an offset. REML will be used for estimation. Maintenance baseline is used in the model as compared to baseline at visit 1. See section 5.7 for details regarding changes as compared to the protocol.

Number of relapses will be summarised by treatment group. Rates (number of relapses divided by patient years of exposure multiplied by 100) will also be presented.

In addition, the distribution of the relapse rate by treatment group will be presented.

Sensitivity analysis:
The number of relapses will be analysed with a negative binomial regression model with treatment group, pooled sites, and disease severity at maintenance baseline as factors, subject as random effect, and time at risk as an offset. REML will be used for estimation. The purpose of this sensitivity analysis is to account for potential overdispersion in data, which is not adjusted for in the Poisson model.

See section 5.7 for details regarding changes as compared to the protocol.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.4.3 Exploratory Assessments

The exploratory assessments collected in the maintenance phase will be summarised for the full analysis set and the exploratory assessments collected in the open-label phase will be summarised for the open-label full analysis set. For all exploratory assessments the observations at visit 2 will be used for the purpose of summarising the change from visit 1 in the open-label phase.

5.4.3.1 Proportion of subjects still at risk of first relapse at week 26 and week 52

In section 11.3.3.3 of the protocol on the analysis of the primary endpoint, it is described that the proportion of subjects still at risk for a first relapse will be compared between the two treatment groups at 26 weeks and 52 weeks after randomisation. This will be considered as two explorative endpoints on its own. The comparison will be done by using an unpaired z-test. In addition, a binomial test will be done. The proportions and the corresponding standard errors will be obtained from the estimated survival curves for the primary endpoint. The estimates of proportions, the 95% confidence intervals and p-value will be presented.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.4.3.2 m-PASI

Open-label phase:
m-PASI will be summarised by visit. Change and percent change in m-PASI from visit 1 to visit 2 will also be summarised.

Maintenance phase:
m-PASI when the subject is not initiating, ending or in a relapse period will be summarised by visit and by treatment group.

m-PASI collected when the subject is initiating a relapse period will be summarised by visit and visit intervals and by treatment group.

m-PASI collected when the subject is ending a relapse period will be summarised by visit and visit intervals and by treatment.

Change and percent change in m-PASI from start of relapse to end of relapse will be summarised by visit for start of relapse and by treatment group.

m-PASI collected at visits where the subject is in a relapse period, will be listed only.

See section 5.7 for details regarding changes as compared to the protocol.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.4.3.3 Physician's Global Assessment of Disease Severity

Open-label phase:
Physician's global assessment of disease severity (PGA) will be summarised by visit. A shift table for categories of PGA at visit 1 versus the category at visit 2 will also be done.

Maintenance phase:
PGA collected when the subject is not initiating, ending or in a relapse period will be summarised by visit and by treatment group.

PGA collected when the subject is initiating a relapse period will be summarised by visit and visit intervals and by treatment group.

PGA collected when the subject is ending a relapse period will be summarised by visit and visit intervals and by treatment group.

A shift table for categories of PGA at start of relapse versus the category at end of relapse will also be done by visit for start of relapse and by treatment group.

PGA collected at visits in the maintenance phase, when the subject is in a relapse period will be listed only.

See section 5.7 for details regarding changes as compared to the protocol.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.4.3.4 Subjects in remission at each visit

The number of subjects in remission will be summarised as described in the protocol section 11.3.4.2 for scheduled visits.

A stack plot over subjects in remission by scheduled visits will be presented.

Further details for the table can be found in Appendix I and Appendix II.

5.4.3.5 Time to when PASI75 is no longer fulfilled

The endpoint will not be analysed. See section 5.7 regarding details of changes as compared to the protocol.

5.4.3.6 Time to first relapse according to m-PASI

The endpoint will not be analysed. See section 5.7 regarding details of changes as compared to the protocol.

5.4.3.7 Efficacy after treatment of relapse

Efficacy after treatment of relapse is defined as the proportion of subjects with 'clear' or 'almost clear' according to the PGA after treatment of relapse. The endpoint will be summarised as described in section 11.3.4.5 of the protocol.

A stack plot over proportion of subjects with 'clear' or 'almost clear' according to the PGA after treatment of relapse by treatment group and relapse number will be presented.

More details for the table can be found in Appendix I and Appendix II.

5.4.3.8 Target lesion/location scores

Open-label phase:
Target lesion/location will be summarised by visit. A shift table for categories of target lesion/location scores at visit 1 versus the category at visit 2 will also be done.

Maintenance phase:
Target lesion/location scores collected when the subject is not initiating, ending or in a relapse period will be summarised by visit and by treatment group.

Target lesion/location scores collected when the subject is initiating a relapse period will be summarised by visit and visit intervals and by treatment group.

Target lesion/location scores collected when the subject is ending a relapse period will be summarised by visit and visit intervals and by treatment group.

A shift table for categories of target lesion/location scores at start of relapse versus the category at end of relapse will also be done by visit for start of relapse and by treatment group.

Target lesion/location scores collected when the subject is in a relapse period will be listed only.

See section 5.7 for details regarding changes as compared to the protocol.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.4.3.9 Body Surface Area

Body surface area (BSA) should be interpreted as the percentage of BSA affected by psoriasis.

Open-label phase:
The percentage of BSA affected by psoriasis will be summarised by visit. Change and percent change in the affected BSA from visit 1 to visit 2 will also be summarised.

Maintenance phase:
The percentage of BSA affected by psoriasis collected when the subject is not initiating, ending or in a relapse period will be summarised by visit and by treatment group.

The percentage of BSA affected by psoriasis collected when the subject is initiating a relapse period will be summarised by visit and visit intervals and by treatment group.

The percentage of BSA affected by psoriasis collected when the subject is ending a relapse period, will be summarised by visit and visit intervals and by treatment group.

Change and percent change in the affected BSA from start of relapse to end of relapse will be summarised by visit for start of relapse and by treatment group.

The percentage of BSA affected by psoriasis collected when the subject is in a relapse period, will be listed only.

See section 5.7 for details regarding changes as compared to the protocol.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.4.3.10 Number of active treatment days during maintenance phase

The number of active treatment days during maintenance phase will be normalised by time of exposure and summarised by treatment group.

For the active treatment group, the number of active treatment days is calculated as the sum of days where treated with maintenance treatment (twice weekly) and days where treated with rescue IMP. A day in relapse where treated with both maintenance medication and rescue IMP will count as one active treatment day.

For the vehicle group, the number of active treatment days during the maintenance phase is calculated as the sum of days where treated with rescue IMP.

The number of active treatment days during maintenance phase will also be listed.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.4.4 Patient-Reported Outcomes

Patient reported outcomes collected in the maintenance phase will be analysed for the full analysis set. Patient reported outcomes collected in the open-label phase will be analysed for the open-label full analysis set.

5.4.4.1 Dermatology Life Quality Index (DLQI)

Open-label phase:
Dermatology life quality index (DLQI) will be summarised by visit. Change and percent change in DLQI from visit 1 to visit 2 will also be summarised.

Maintenance phase:
DLQI collected when the subject is not initiating, ending or in a relapse period will be summarised by visit and by treatment group.

DLQI collected when the subject is initiating a relapse period will be summarised by visit and visit intervals and by treatment group.

DLQI collected when the subject is ending a relapse period will be summarised by visit and visit intervals and by treatment group.

Change and percent change in DLQI from start of relapse to end of relapse will be summarised by visit for start of relapse and by treatment group.

DLQI collected when the subject is in a relapse period will be listed only.

See section 5.7 for details regarding changes as compared to the protocol.

Details on total DLQI scores calculation:
The total DLQI score will be presented in all above mentioned tables. The total DLQI score is calculated by summing the score of each question. If one question is left unanswered, this is scored 0, and the total score is calculated as usual. If two or more questions are left unanswered, no total score is calculated. The questions 1-6 and 8-10 are scored as described in Table 4. Question 7 is scored as described in Table 5. The total DLQI score ranges from 0 (no quality of life impairment) to 30 (maximal quality of life impairment).

Table 4: Scoring of DLQI question 1-6 and 8-10

Answer	**Score**
Very much	3
A lot	2
A little	1
Not at all	0
Not relevant	0
Unanswered	0

Table 5: Scoring of DLQI question 7

Answer		**Score**
Main part of question 7	**Subpart of question 7**	
Yes	Unanswered	3
Not relevant	Unanswered	0
No	A lot	2
No	A little	1
No	Not at all	0
No	Unanswered	0

If the main part of question 7 is answered with ‘Yes’, and the subpart is not left unanswered, the score will remain 3. If the main part of question 7 is answered with ‘Not relevant’, and the

subpart of the question is answered with 'A lot' or 'A little', the score will be 2 or 1 respectively.

Multiple imputation:
Missing DLQI total scores will be imputed using multiple imputation with 100 copies (seed=70309491) described in the steps below.

Missing assessment of the DLQI total score in-between non-missing assessments in the maintenance phase will not be imputed. The imputation step will depend on whether the reason for withdrawal for the subject to be imputed could potentially be related to IMP or not.

Imputation for subjects withdrawn with reasons 'withdrawal by subject' or 'lost to follow up':
This approach assumes that in the unobserved part of maintenance phase, the subject will behave similar to the observed part of the maintenance phase for subjects in the same treatment group completing the maintenance phase.

Imputation steps:

1. DLQI data and relapse status from one subject in the sub-set of subjects that completed their maintenance phase and are in the same treatment group as the withdrawn subject will be randomly selected. This will be referred as 'sampled data' in step 2.
2. Missing visits for the withdrawn subject will be inputted using the relevant visits from the sampled data.
3. Steps 1 and 2 will be repeated 100 times for each withdrawn subject to form 100 complete datasets

Imputation subjects withdrawn with reasons 'adverse event', 'death', 'lack of efficacy', or 'subject not achieving clear or almost clear after treatment of relapse':
This approach assumes that the subjects behave similarly in the unobserved part of the trial as the observed part for subjects leaving the trial for the same reasons independent of treatment group.

Imputation steps:

1. Total DLQI scores and corresponding relapse status from subjects withdrawn from the trial due to 'adverse event', 'death', 'lack of efficacy', or 'subject not achieving clear or almost clear after treatment of relapse' will be collected as one set of data.

2. A total DLQI scores will be sampled for each scheduled visit from the above collection of data (step 1).
3. Steps 1 and 2 will be repeated 100 times for each withdrawn subject to form 100 complete datasets

Imputation for subjects leaving the trial due to other reasons:
For cases with withdrawal reason specified as 'Other', the details will be revised on a blinded manner, selecting and documenting the imputation approach in the Analysis Set Definition Document.

Statistical analysis:
For each of the 100 complete datasets the total DLQI scores will be analysed using a Mixed effect Model Repeated Measurement (MMRM) with treatment group, visit (scheduled), interaction between treatment and visit, relapse status, and maintenance baseline total DLQI score as fixed factors and subject as random effect. Repeated measurements within subject is modelled using an unstructured variance structure. REML will be used for estimation.

The estimates and standard errors from the 100 analyses will be pooled into estimated least squares means for each treatment group and estimated treatment difference with associated standard errors using Rubin's rule to draw inference. From these pooled treatment estimates, the 95% CI for the treatment difference will be calculated. The p-value for treatment difference will be calculated using a two-tailed Student's t-test based on the pooled estimate. Pooled treatment estimates together with treatment difference, 95% CI and p-value will be presented by visit. Furthermore, the pooled treatment estimates will be plotted by visit.

See section 5.7 for details regarding changes as compared to the protocol.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.4.4.2 EQ-5D-5L-PSO

Open-label phase:
EQ-5D-5L-PSO dimensions, the index score and health on VAS score will be summarised by visit.
A shift table for the category for each of the EQ-5D-5L-PSO dimensions at visit 1 versus the category at visit 2 will be done.
Change and percent change in EQ-5D-5L-PSO index score and health on VAS score from visit 1 to visit 2 will be summarised.

Maintenance phase:
EQ-5D-5L-PSO dimensions, the index score and health on VAS score collected when the subject is not initiating, ending or in a relapse period will be summarised by visit and by treatment group.

EQ-5D-5L-PSO dimensions, the index score and health on VAS score collected when the subject is initiating a relapse period will be summarised by visit and visit intervals and by treatment group.

EQ-5D-5L-PSO dimensions, the index score and health on VAS score collected when the subject is ending a relapse period will be summarised by visit and visit intervals and by treatment group.

A shift table for the category for each of the EQ-5D-5L-PSO dimensions at start of relapse versus the category at end of relapse will also be done by visit for start of relapse and by treatment group.

Change and percent change in EQ-5D-5L-PSO index score and health on VAS score from start of relapse to end of relapse will be summarised by visit for start of relapse and by treatment group.

EQ-5D-5L-PSO dimensions, the index score and health on VAS score collected when the subject is in a relapse period, will be listed only.

See section 5.7 for details regarding changes as compared to the protocol.

More details for the tables and listings can be found in Appendix I and Appendix II.

The index score will be calculated calculated according to:
https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/valuation-standard-value-sets/crosswalk-index-value-calculator/.
The UK value sets will be used. In this way, each possible EQ-5D health state is assigned a weight representing the utility or value of that state, on a scale with a maximum value of 1, representing full health, and an anchor of 0, representing equivalent to being death. Values lower than 0 represent states regarded as worse than being death.

5.4.4.3 WPAI:PSO

The WPAI:PSO questionnaire will be presented by impairment percentages with high number indicating greater impairment. Four derived domains will be constructed from the WPAI:PSO questions (Q1-Q6) as described in Table 6.

Table 6: Scoring of WPAI:PSO question 1-6

Impairment percentage	Score
Absenteeism	Q2/(Q2+Q4)
Presenteeism	Q5/10
Total work productivity impairment (TWPI)	Q2/(Q2+Q4)+(1-Q2/(Q2+Q4))x(Q5/10)
Total activity impairment (TAI)	Q6/10

Open-label phase:
The WPAI:PSO scores will be summarised by visit.
Change and percent change in each WPAI:PSO questions from visit 1 to visit 2 will also be summarised.

Maintenance phase:
The WPAI:PSO scores will be summarised by visit, by treatment group and by whether the subject is on rescue IMP or not. As the WPAI:PSO questionnaire is based on experiences with psoriasis during the past 7 days, a subject will be summarised in the rescue IMP category if the subject has been on rescue IMP in at least one of the past 7 days prior to the visit.
WPAI:PSO scores collected at unscheduled visits will be listed only.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.4.4.4 Psoriasis Symptom Inventory

The total PSI score is calculated by summing the individual item score of each of the eight symptoms. If one question is left unanswered, this is scored 0, and the total score is calculated as usual. If two or more questions are left unanswered, no total score is calculated. The answers are scored as described in Table 7. The total PSI score ranges from 0 (not at all severe psoriasis symptoms) to 32 (very severe psoriasis symptoms).

Table 7: Scoring of PSI questions

Answer	Score
Very severe	4

Answer	**Score**
Severe	3
Moderate	2
Mild	1
Not at all	0
Unanswered	0

Open-label phase:
The AUC for total PSI scores will be calculated. Change and percent change in total PSI score from visit 1 to visit 2 will also be summarised.

The AUC for the PSI total score will be calculated for each subject using the standard trapezoidal rule where trial day is used for the x-axis of the curve and total PSI score is used for the y-axis of the curve. The AUC will be normalised by dividing with the time period from visit 1 to visit 2. The normalisation converts the AUC to the original scale of the total PSI score.

Maintenance phase:
The AUC for the total PSI scores (from randomisation to 28 weeks after randomisation) will be calculated. The AUC for the total PSI score collected in time in remission and time in relapse, respectively, will be summarised by treatment group.

The AUC for the PSI total score for time in remission will be calculated for each subject by summing AUC over the time intervals where the subject is in remission. The AUC will be normalised by the total time the subject is in remission.

Likewise, the AUC for the PSI total score for time in relapse will be calculated for each subject by summing AUC over time intervals where the subject is in relapse. The AUC will be normalised by the total time the subject is in relapse. Missing assessment of the PSI total score in-between non-missing assessments in the maintenance phase will not be imputed, which corresponds to linear interpolation between non-missing assessments of the PSI total score.

Multiple imputation:
Missing DLQI total scores will be imputed using multiple imputation with 100 copies (seed=70309491). The imputation method and the imputation steps are the same as described for DLQI in section 5.4.4.1, however the imputation is done by week and not by visit.

Statistical analysis:
For each of the 100 complete data sets, the total PSI scores will be analysed using a Mixed effect Model Repeat Measurement (MMRM) with treatment group, week (from randomisation), interaction between treatment and week, relapse status, and maintenance baseline total PSI score as fixed factors and subject as random effect. Repeated measurements within subject is modelled using an unstructured variance structure. REML will be used for estimation.

The estimates and standard errors from the 100 analyses will be pooled into estimated least squares means for each treatment group and estimated treatment difference with associated standard errors using Rubin's rule to draw inference. From these pooled treatment estimates, the 95% CI for the treatment difference will be calculated. The p-value for treatment difference will be calculated using a two-tailed Student's t-test based on the pooled estimate. Pooled treatment estimates together with treatment difference, 95% CI and p-value will be presented by week. Furthermore, the pooled treatment estimates will be plotted by week.

Subjects are supposed to complete the PSI questionnaire on a weekly basis the first 28 weeks of the maintenance phase and the 2 last weeks of the maintenance phase (Week 54 to 56) which is only applicable for completers. However, during blind review of data, it is observed that subjects in general forget to complete the questionnaire the last 2 weeks which implies that limited data are available for this period. For this reason, the analysis of the PSI total score will be based on the first 28 weeks of the maintenance phase.

The analysis of PSI will be done for full analysis set.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.4.4.5 Subject's Global Assessment of Disease Severity (SGA)

Open-label phase:
Subject's global assessment of disease severity (SGA) will be summarised by visit.
A shift table for categories of subject's global assessment of disease severity at visit 1 versus the category at visit 2 will also be done.

Maintenance phase:
SGA collected when the subject is not initiating, ending or in a relapse period will be summarised by visit and by treatment.

SGA collected when the subject is initiating a relapse period, will be summarised by visit and visit intervals and by treatment.

SGA collected when the subject is ending a relapse period will be summarised by visit and visit intervals and by treatment group.

A shift table for categories of SGA at start of relapse versus the category at end of relapse will also be done by visit for start of relapse and by treatment group.

SGA collected when the subject is in a relapse period will be listed only.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.5 Analysis of Safety

The analyses of safety is done for the open-label safety analysis set and the safety analysis set.

5.5.1 Exposure

Duration of exposure will be summarised as described in the protocol section 11.3.3.1. If the date of last application of IMP is missing, the date of last visit attended by the subject will be used instead.

Patient years of exposure during a trial phase will be calculated as exposure during the relevant phase (accounting for both maintenance and rescue IMP as relevant) divided by 365.25.

The amount of IMP used will be summarised for the open-label treatment phase. For each subject the amount of IMP used will be normalised by the length of the open-label phase.

The total amount of IMP used, and the amount of rescue IMP used will be summarised by treatment group for the maintenance phase. For each subject the total amount of IMP and the amount of IMP used will be normalised by the length of maintenance phase or the total time in relapse, respectively.

The amount of IMP used, and the amount of rescue will not be summarised for each visit interval as described in the protocol. Instead a cumulative plot of the amount of IMP used over time during the maintenance phase by each subject together with an average cumulative amount curve will be done for the safety analysis set. The cumulative amount of IMP for each subject will be normalised by time in the maintenance phase (in days). The cumulative

amount of IMP used up to each scheduled visit and the corresponding number of subjects contributing to these amounts will be tabulated by treatment group.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.5.2 Drug Accountability

For each subject, the weight of IMP used for a given trial period will be calculated as the difference between the weight of a set of full cans dispensed and the weight of the returned cans. The weight of cans dispensed to a subject will be the mean weight of a full can multiplied by the number of dispensed cans. The mean weight of a full can is 195.52 g based on the weight of 20 cans. The weight of IMP used will be multiplied by a correction factor of 0.41 to account for the propellant gasses.

If cans are returned with their seal unbroken, the weight of IMP used from that bottle will be assigned a value of zero. If a returned can weigh more than the estimated mean weight of a full can, it will be assumed that zero grams were used from that can.

If cans are returned at a wrong visit the amount of IMP used from these cans will be assumed to be used in the period from the cans being dispensed to the cans being returned. If some cans are not returned at all, these are cans are assumed to be emptied by the subjects. The amount of IMP used for that bottle will be assigned a value of 60 g, which is the approved amount of IMP contained in an individual can.

In the case where cans are not returned due to the subjects being lost to follow up after the cans is dispensed, the amount of IMP used from these cans will not be calculated, as the subject is assumed to end the treatment with IMP after withdrawal from the trial.

5.5.3 Adverse Events

The adverse events (AEs) will be assigned to a specific period (e.g. open-label phase or randomised phase) based on the onset date the AE.

The long-term safety of LEO 90100 will be evaluated based on data from the randomised phase.
For treatment emergent adverse events (hereafter referred to as AEs) occurring in the randomised phase the following tables will be done:

An overall summary of AEs, SAEs, premature discontinuation from the trial due to AEs, treatment related AEs, severity of AEs, action taken with IMP and outcome of AEs will be presented. The summary will include number of events, number (percentage) of subjects and exposure rates.

The number of AEs, the number and percentage of subjects experiencing each type of AE, and the exposure rate will be tabulated by SOC and preferred term. The tabulation will be done for all treatment emergent AEs, for each type of severity separately, for related AEs, for serious AEs (SAEs), for non-serious adverse events, and for frequent AEs (>= 1% in any treatment group).

All above tables will be done for the safety analysis set by treatment for the first 28 weeks of the randomised phase, and for the remaining 32 weeks of the randomised phase separately. In addition, the tables will be done for the safety analysis set by randomised treatment and rescue IMP for the total randomised phase, for the first 28 weeks of the randomised phase, and for the remaining 32 weeks of the randomised phase separately.

Further details for the tables can be found in Appendix I and Appendix II.

Open-label phase:
For completeness, AEs for the open-label phase will be summarised separately as follows:

An overall summary of AEs, SAEs, AEs leading to withdrawal, treatment related AEs, severity of AEs, action taken with IMP and outcome of AEs will be presented. The summary will include number of events, number (percentage) of subjects and exposure rates.

The number of AEs, the number and percentage of subjects experiencing each type of AE, and the exposure rate will be tabulated by SOC and preferred term. The tabulation will be done for all treatment emergent AEs, for each type of severity separately, for related AEs, for serious AEs (SAEs), for non-serious adverse events, and for frequent AEs (>= 1%).

The causal relationship to trial medication for each type of AE will be tabulated by SOC and preferred term.

All above tables will be done for the open-label safety analysis set.

Additional summaries in the maintenance phase:
Tables exploring safety profile while in remission or relapse will be presented based on the treatment emergent adverse events occurring in the maintenance phase.

For AEs from the maintenance phase the following tables will be done:

The number of AEs, the number and percentage of subjects experiencing each type of AE, and the exposure rate will be tabulated by SOC and preferred term. The tabulation will be done for all treatment emergent AEs, for each type of severity separately, for related AEs, for serious AEs (SAEs), for non-serious adverse events, and for frequent AEs (>= 1% in any treatment group). The causal relationship to treatment regimen for each type of AE will be tabulated by SOC and preferred term.

All above tables will be done for the safety analysis set by treatment for the first 28 weeks of the maintenance phase, and for the remaining 24 weeks of the maintenance phase separately. In addition, the tables will be done for the safety analysis set by randomised treatment and rescue IMP for the total maintenance phase, for the first 28 weeks of the maintenance phase, and for the remaining 24 weeks of the maintenance phase separately.

All non-treatment emergent AEs will be listed.

Further details for listings can be found in Appendix I.

Statistical tests:
In the protocol it is described that the percentage of subjects with any AE or with any related AE will be compared between treatment groups by a chi-square test or Fisher's exact test (if expected cell count < 5). However, this analysis will most likely be biased towards different drop-out between the treatment groups. The longer a subject is followed, the greater is the chance of observing an AE for the subject. As the number of early withdrawals might differ considerably between the two treatment groups, statistical tests performed on the percentage of subjects with any AE or with any related AE is not appropriate in this set up. Hence, no statistical testing will be done for AEs.

Calculation of AE rate:
The AE rate will be calculated as number of AEs divided by patient years of exposure in the different phases multiplied by 100.

5.5.3.1 Adverse events associated with long term corticosteroid use

Adverse events associated with long term corticosteroid use will be presented as described in the protocol.

5.5.4 Rebound

Rebounds will be defined as described in the protocol. The baseline value will be the m-PASI value measured at the start of the rebound follow-up period. A rebound follow-up period is defined as either (i) 2 months after discontinuation of open-label phase treatment, (ii) 2 months after discontinuation of relapse treatment, or (iii) 2 months after discontinuation of maintenance treatment (up to Visit FU3).

Number of rebounds occurring within the first 2 months after discontinuation of the open-label phase treatment, and number of rebounds occurring within 2 months after discontinuation of relapse treatment will be summarised by treatment group.

Number of rebounds occurring within two months after discontinuation of maintenance treatment will be summarised by treatment group.

Cases of rebounds will be listed.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.5.5 Physician's Assessment of Local Safety and Tolerability

Open-label phase:
Physician's assessment of local safety and tolerability will be summarised by visit.
A shift table for categories of physician's assessment of local safety and tolerability at visit 1 versus the category at visit 2 will also be done.

Maintenance phase:
Physician's assessment of local safety and tolerability when the subject is not initiating, ending or in a relapse period will be summarised by visit and by treatment group.

Physician's assessment of local safety and when the subject is initiating a relapse period will be summarised by visit and visit intervals and by treatment group.

Physician's assessment of local safety and tolerability when the subject is ending a relapse period will be summarised by visit and visit intervals and by treatment group.

A shift table for categories of physician's assessment of local safety and tolerability at start of relapse versus the category at end of relapse will also be done by visit for start of relapse and by treatment group.

Physician's assessment of local safety and tolerability collected when subject is in a relapse period, will be listed only.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.5.6 Subject's Assessment of Local Safety and Tolerability

Open-label phase:
Subject's assessment of local safety and will be summarised by visit. A shift table for categories of subject's assessment of local safety and tolerability at visit 1 versus the category at visit 2 will also be done.

Maintenance phase:
Subject's assessment of local safety and tolerability collected when the subject is not initiating, ending or in a relapse period will be summarised by visit and by treatment group.

Subject's assessment of local safety and tolerability collected when the subject is initiating a relapse period will be summarised by visit and visit intervals and by treatment group.

Subject's assessment of local safety and tolerability collected when the subject is ending a relapse period will be summarised by visit and visit intervals and by treatment group.

A shift table for categories of subject's assessment of local safety and tolerability at start of relapse versus the category at end of relapse will also be done by visit for start of relapse and by treatment group.

Subject's assessment of local safety and tolerability collected when the subject is in a relapse period, will be listed only.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.5.7 ACTH-Challenge Test

Open-label phase:
For the group of subjects undergoing the ACTH-challenge test, the number and percentages of subjects with serum-cortisol concentration values ≤18 mcg/dl at 30 minutes and 60 minutes after the ACTH-challenge test will be summarised by visit.

The serum-cortisol concentration at time 0 (just before the ACTH-challenge test) and at 30 and 60 minutes after ACTH-challenge at visit 1 and visit 2 will be summarised.

Individual data for subjects with serum cortisol concentration values ≤18 mcg/dl at either 30 or at 60 minutes after ACTH-challenge in the open-label phase will be tabulated.

A mean plot of the serum-cortisol concentration at time 0, and at 30 and 60 minutes after the ACTH-challenge test for visit 1 and visit 2 will be done.

Maintenance phase:
The number and percentages of subjects with serum-cortisol concentration values ≤18 mcg/dl at 30 minutes and 60 minutes after the ACTH-challenge test will be summarised by visit and by treatment group.

The serum-cortisol concentration at time 0 and at 30 and 60 minutes after ACTH-challenge tests will be summarised by visit and treatment group.

Individual data for subjects with serum cortisol concentration values ≤18 mcg/dl at either 30 or at 60 minutes after ACTH-challenge will be tabulated.

A mean plot of the serum-cortisol concentration at time 0, and at 30 and 60 minutes after the ACTH-challenge test by treatment group will be done.

Results from ACTH-tests performed at early termination visits will be listed only and are not included in the above-mentioned tables and figures.

More details for the tables and listings can be found in Appendix I and Appendix II.

5.5.8 Vital Signs and Physical Findings

Open-label phase:
The change in vital signs (blood pressure, heart rate) from baseline to end of open-label treatment phase will be summarised.

Maintenance phase:
The change in vital signs (blood pressure, heart rate) from randomisation to end of trial will be summarised.

In addition, the change in vital signs from randomisation to end of maintenance phase for subjects discontinuing before 6 months after randomisation, the change in vital signs from randomisation to end maintenance phase for subjects discontinuing on or after 6 months after

randomisation, and the change in vital signs from randomisation to visit 15 will be summarised.

If more than one vital sign value is reported for the same visit and time point, the latest value will be used in summary statistics and analyses.

If vital sign measurements are missing for a subject at baseline or at randomisation the change from baseline or randomisation to a specific visit will not be calculated.

Further details for the tables can be found in Appendix I and Appendix II.

Findings from physical examinations and vital signs data will be listed. More details can be found in Appendix I.

5.5.9 Laboratory Data

For the laboratory values, if the value is below the lower limit of quantification, half of the lower limit will be used for quantitative summaries. If the value is above the upper limit of quantification, the upper limit value will be used. If more than one laboratory value is reported for the same visit, the latest value will be used in summary statistics and analyses.

If laboratory parameters are missing for a subject at baseline or at randomisation the change from baseline or randomisation to a specific visit will not be calculated.

Laboratory parameters will be categorised as described in the protocol.

Open-label phase:
The change in each of the laboratory parameters from baseline to end of open-label treatment phase will be summarised. A shift table for categories of laboratory parameters at visit 1 versus the category at visit 2 will also be done.

Maintenance phase:
The change in laboratory parameters from randomisation to end of maintenance phase for subjects discontinuing before 6 months after randomisation, the change in laboratory parameters from randomisation to end of maintenance phase for subjects discontinuing on or after 6 months after randomisation, and the change in laboratory parameters from randomisation to visit 15 will be summarised.

Shift tables showing the categories at randomisation against those at end of maintenance phase for subjects discontinuing before 6 months after randomisation, for subjects discontinuing the trial on or after 6 months after randomisation, and for subjects completing the maintenance phase will be produced.

For subjects with at least one clinically significant value of albumin corrected serum calcium, similar shift tables as described above will be produced.

All laboratory data will be listed. Additionally, subjects with laboratory parameters outside the reference range will be listed in a separate listing.

Further details for the tables and listings can be found in Appendix I and Appendix II.

5.6 General Principles

5.6.1 Pooling of Trial Sites

As many centres randomises only a few subjects, the centres will be pooled together. For the United States, due to the large geographical area and diverse climatic conditions, centres will be pooled with neighbouring centres based on graphical location and climatic zones to form two pooled centres. The pooling of sites is shown in Table 8.

Table 8: Pooling of trial sites

Country	**Number of subjects randomised**	**Pooled sites**
Canada	132	CAN140, CAN142, CAN143, CAN144, CAN145, CAN146, CAN147, CAN148, CAN149, CAN150, CAN152, CAN154
France	55	FRA160, FRA161, FRA162, FRA165, FRA167
Germany	52	DEU183, DEU185, DEU186, DEU187, DEU188, DEU189, DEU193
Great Britain	68	GBR200, GBR201, GBR202, GBR203, GBR207, GBR209, GBR210

Poland	56	POL220, POL221, POL222, POL224
United States (1)	68	USA103, USA106, USA109, USA112, USA122
United States (2)	114	USA100, USA102, USA104, USA107, USA108, USA110, USA111, USA113, USA115, USA116, USA117, USA118, USA119, USA120, USA121

5.6.2 Handling of Drop-outs and Missing Values

The methods of dealing with drop-outs and missing values for primary and secondary endpoints are specified in the relevant sections of the statistical analysis plan, where the analyses of the endpoints are described. If nothing is specified in these sections, missing data and drop-outs are not an issue of concern for the analyses of the endpoint and nothing will be done.

5.6.3 Incomplete dates

For incomplete start dates of adverse events in data, the following rules apply:

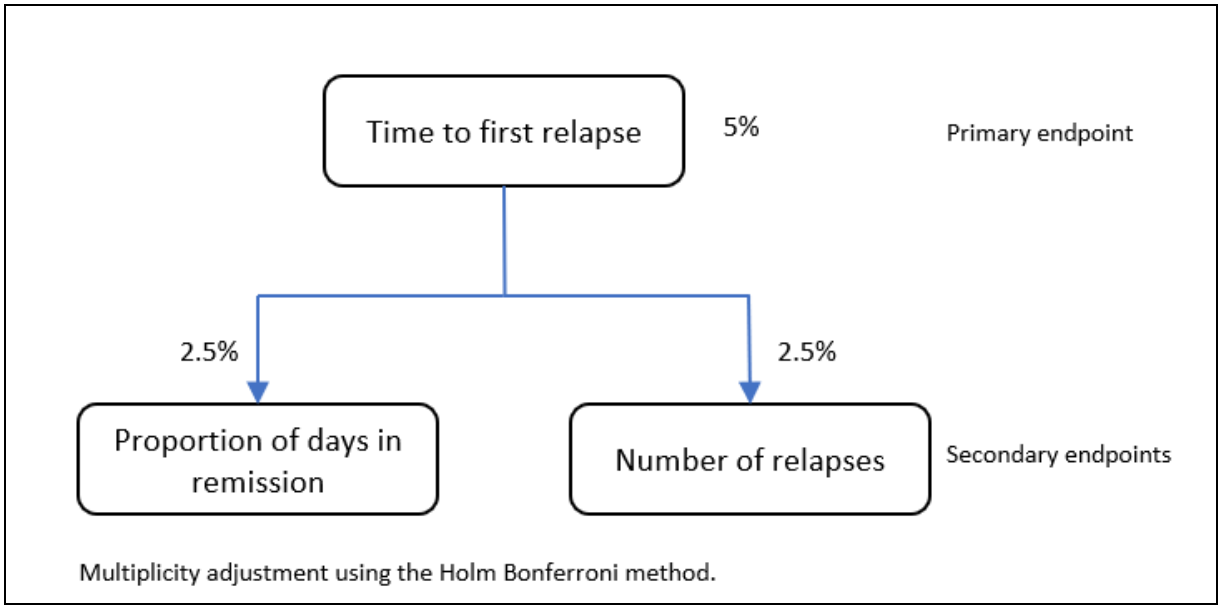
- If a start day is missing, but start month and year is not missing, it will be assumed that the start date of the adverse event is the date of last contact with the subject in that month, if available, and otherwise it will be the first day of the month.
- If both start day and month is missing, it will be assumed that the start date of the adverse event is the date of the last contact with the subject before the end date of the adverse event.

The adverse events will be assigned to rescue medication and randomised treatment as described in section 5.5.3 based on the imputed dates derived from the above rules.

5.6.4 Multiplicity adjustment

To control the overall type 1 error rate, the analyses of the primary and secondary endpoints will follow the hierarchical testing procedure outlined in Figure 3. The hypotheses relating to the two secondary endpoints cannot be rejected unless the hypothesis relating to the primary endpoint is also rejected.

Figure 3: Testing procedure for primary and secondary endpoints



The procedure will be as follows:
Time to first relapse between LEO 90100 and vehicle is evaluated at a 5% significance level. If the test is significant, the significance level will be split between the analyses of the two secondary endpoints using the Holm Bonferroni method to adjust for multiplicity. Hence the proportion of days in remission and the number of relapses during the maintenance phase between LEO 90100 and vehicle will be tested in parallel at a 2.5% significance level.

5.6.5 Treatment Labels

The treatment labels for the clinical trial report text and tables are shown in Table 9.

Table 9: Treatment labels for the clinical trial report text and tables

Label Used in Text	Label Used in Tables	Order in Table
LEO 90100 aerosol foam	LEO 90100	1
LEO 90100 aerosol foam vehicle	Vehicle	2

5.7 Changes to the analyses described in the protocol

The following changes have been done to the analyses described in the protocol:

SAP section	Endpoint/Assessment	Description of change
Section 5.3.4	Compliance	Data captured in the eDiary will not allow the computation of percentage missed application in the maintenance phase as described in the protocol (section 11.3.3.2). Number of subjects in non-compliance with maintenance treatment instructions (i.e.; excluding relapse periods) will be summarised by treatment group.
Section 5.4.1	Time to first relapse (primary endpoint)	The analysis described in the protocol includes disease severity at baseline (visit 1) as a covariate and trial site as a factor in the model (section 11.3.3.3). In the SAP the disease severity at maintenance baseline and pooled sites are included in the model instead. A sensitivity analysis is added in the SAP, where the primary endpoint will be analysed incorporating interval censoring. As compared to the primary analysis assuming that the start of relapse is known, the sensitivity analysis assumes the relapse starts between two visits. The analysis of subjects who are still at risk for a first relapse at week 26

		and 52 mentioned in the protocol section 11.3.3.3 are described as two addition exploratory efficacy endpoints in section 5.4.3.1.
Section 5.4.3.1	Proportion of subjects who are still at risk of a first relapse at week 26. Proportion of subjects who are still at risk of a first relapse at week 52.	These two endpoints where mentioned in section 11.3.3.3 of the protocol. In the SAP they are added as exploratory endpoints.
Section 5.4.2.1	Proportion of days in remission	Analysis of number of days in remission is described in the protocol (section 11.3.3.6). The length of the maintenance phase will vary from subject to subject and will influence the number of days in remission. Due to this reason, the endpoint in SAP has been changed to the proportion of days in remission. The imputation method described in the protocol section 11.3.3.6 is not done, since if the withdrawal rate is higher in the vehicle arm (due to lower efficacy), the approach would favour the active treatment arm. In the SAP a multiple imputation method is described instead. See section 5.4.2.1 for details.
Section 5.4.2.2	Number of relapses during the maintenance phase.	The analysis described in the protocol includes disease severity at baseline (visit 1) as a covariate and trial site as a factor in the model (section

		11.3.3.6). In the SAP the disease severity at maintenance baseline and pooled sites are included in the model instead. Sensitivity analysis: The analysis described in the protocol (section 11.3.3.6) will not be done as it conditions on future events by excluding subjects who at some point do not achieve 'clear' or 'almost' clear according to PGA after treatment of relapse. A negative binomial regression model will be used for the analysis instead. See section 5.4.2.2 for details.
Sections 5.4.3.2	m-PASI	In the protocol section 11.3.4.1 it is described that the endpoint will be summarised by visit. Since per protocol subjects will be withdrawn when not achieving 'clear' or 'almost clear' according to PGA after rescue IMP, the subset of subject's available values at the visits will be a selected population (most likely are subjects who responds well to the IMP). Hence summaries by visit will not be done. The summaries will be done only for data capture at the start or the end of a relapse period. See section 5.4.3.2.
Section 5.4.3.3	Physician's Global Assessments of disease severity	This endpoint is added as compared to the protocol. The summaries will be done only for data capture at the start or the end of a relapse period. See section 5.4.3.3 for details.

Section 5.4.3.5	Time to when PASI75 is no longer fulfilled	PASI and PGA are both tools for assessing the psoriasis severity and will therefore be mutually related. Since rescue IMP will be given to patients in relapse (based on the PGA) y, the level of PASI might also be affected. Therefore, the observed progress in PASI over time might be confounded with the rescue IMP. For this reason, time to when PASI75 is no longer fulfilled, will not be analysed (protocol section 11.3.4.3).
Section 5.4.3.6	Time to first relapse according to m-PASI	m-PASI and PGA are both tools for assessing the psoriasis severity and will therefore be mutually related. Since rescue IMP will be given to patients in relapse (based on the PGA) y, the level of m-PASI might also be affected. Therefore, the observed progress in m-PASI over time might be confounded with the rescue IMP. For this reason, time to first relapse according to m-PASI, will not be analysed (protocol section 11.3.4.4).
Section 5.4.3.8	Target lesion/location scores	In the protocol section 11.3.4.6 it is described that the endpoint will be summarised by visit. Since per protocol subjects will be withdrawn when not achieving ‘clear’ or ‘almost clear’ according to PGA after rescue IMP, the subset of subject’s available values at the visits will be a selected population (most likely are subjects who responds well to the IMP). Hence summaries by visit will not be done. The summaries will be done only for data capture at the start or the end of a relapse period. See section 5.4.3.8.

Section 5.4.3.9	Body surface area	In the protocol section 11.3.4.7 it is described that the endpoint will be summarised by visit. Since per protocol subjects will be withdrawn when not achieving 'clear' or 'almost clear' according to PGA after rescue IMP, the subset of subject's available values at the visits will be a selected population (most likely are subjects who responds well to the IMP). Hence summaries by visit will not be done. The summaries will be done only for data capture at the start or the end of a relapse period. See section 5.4.3.9.
Section 5.4.4.1	Total DLQI score	In the protocol section 11.3.5.1 it is described that the endpoint will be summarised by visit. Since per protocol subjects will be withdrawn when not achieving 'clear' or 'almost clear' according to PGA after rescue IMP, the subset of subject's available values at the visits will be a selected population (most likely are subjects who responds well to the IMP). Hence summaries by visit will not be done. The summaries will be done only for data capture at the start or the end of a relapse period. See section 5.4.4.1. The analysis described in the protocol section 11.3.5.1 disregard the possible differences in withdrawal patterns between the two treatment groups. Instead multiple imputation for missing data and an MMRM analysis will be done. See section 5.4.4.1 for details.

Section 5.4.4.2	EQ-5D-5L PSO	In the protocol section 11.3.5.2 it is described that the endpoint will be summarised by visit. Since per protocol subjects will be withdrawn when not achieving 'clear' or 'almost clear' according to PGA after rescue IMP, the subset of subject's available values at the visits will be a selected population (most likely are subjects who responds well to the IMP). Hence summaries by visit will not be done. The summaries will be done only for data capture at the start or the end of a relapse period. See section 5.4.4.2.
Section 5.4.4.4	PSI	In the protocol section 11.3.5.1 it is described that the endpoint will be summarised over time. Since per protocol subjects will be withdrawn when not achieving 'clear' or 'almost clear' according to PGA after rescue IMP, the subset of subject's available values over time in the trial will be a selected population (most likely are subjects who responds well to the IMP). Hence summaries over time will not be done. The summaries will be done using AUC over trial phases. See section 5.4.4.4 for details. The analysis described in the protocol section 11.3.5.4 disregard the possible differences in withdrawal patterns between the two treatment

		groups. Instead multiple imputation for missing data and an MMRM analysis will be done. See section 5.4.4.1 for details.
Section 5.4.4.5	SGA	In the protocol section 11.3.5.5 it is described that the endpoint will be summarised by visit. Since per protocol subjects will be withdrawn when not achieving 'clear' or 'almost clear' according to PGA after rescue IMP, the subset of subject's available values at the visits will be a selected population (most likely are subjects who responds well to the IMP). Hence summaries by visit will not be done. The summaries will be done only for data capture at the start or the end of a relapse period. See section 5.4.4.5.

Appendix I

Tables, Figures and Listings

Tables and Figures, Baseline Characteristics and Investigational Product Data (Module 2)

Tables

Figures

Tables and Figures, Efficacy Data (Module 3)

Tables

Primary Efficacy Endpoint

Secondary Efficacy Endpoints

Exploratory Efficacy Endpoints

Patient-Reported Outcomes

Figures

Tables and Figures, Safety Data (Module 4)

Tables

Figures

Patient Data Listings (Appendix 1)

Patient Data Listings (Appendix 2)

Appendix 2.3: Trial Analysis Sets

Listing 3-1. Trial Analysis Set

Listing 3-2. Reasons for Exclusion from Analysis Set

Appendix 2.4: Demographic Data

Listing 4-1. Demographics

Listing 4-2. Date/Age of First Diagnosis of Psoriasis

Listing 4-3. Actual Trial Period

Listing 4-4. Medical History

Listing 4-5. Concurrent Diagnoses at Baseline

Listing 4-6. Concomitant Medication

Listing 4-7. Concurrent Procedures

Listing 4-8. Previous Anti-Psoriatic Treatment

Listing 4-9. Location of Psoriasis

Listing 4-10. Location of other Psoriasis

Appendix 2.5: Compliance and/or Investigational Product Concentration Data

Listing 5-1. Administration of Investigational Product

Listing 5-2. Drug Accountability

Appendix 2.6: Efficacy Data

Listing 6-1. Dermatology Quality Life Index

Listing 6-2. EQ-5D-5L-PSO

Listing 6-3. Work Productivity and Activity Impairment: Psoriasis (WPAI:PSO)

Listing 6-4. Psoriasis Symptom Inventory (PSI)

Listing 6-5. Physician's Global Assessment of Disease Severity (PGA)

Listing 6-6. Physician's Assessment of the Extent and Severity of Clinical Signs (m-PASI)

Listing 6-7. Investigator's Assessment of Body Surface Area (BSA)

Listing 6-8. Subject's Global Assessment of Disease Severity (SGA)

Listing 6-9. Target Lesion/Location Score

Listing 6-10. Number of Active Treatment Days during the Maintenance Phase

Listing 6-11. Time to First Relapse

Listing 6-12. Proportion of Days in Remission

Listing 6-13. Number of Relapses

Appendix 2.7: Safety Data

Listing 7-1. Deaths

Listing 7-2. Serious Adverse Events

Listing 7-3. Subjects withdrawn from trial due to Adverse Events

Listing 7-4. Severe Adverse Events

Listing 7-5. Adverse Events

Additional Tables for Results Reporting in Clinical Trial Data Registries

Table 4-1 Non-serious AEs occurring in ≥1% subjects by MedDRA primary SOC and preferred term: open-label safety analysis set

Table 4-2 Non-serious AEs occurring in in ≥1% subjects by MedDRA primary SOC and preferred term: safety analysis set

Table 4-3 Serious AEs by MedDRA primary SOC and preferred term: open-label safety analysis set

Table 4-4 Serious AEs by MedDRA primary SOC and preferred term: safety analysis set

Table 4-5 Subject enrolment and treatment assigned: enrolled subjects and subjects assigned treatment

Appendix II

Shells

Shell 1: Disposition of subjects in the open-label phase: enrolled subjects

	Open-label LEO 90100 (n=xxx)	
	N (%)	Visit 2 (Week 4) attendance Yes / No
Enrolled subjects	xx(xx.x)	xx / xx
Randomised subjects	xx(xx.x)	xx / xx
Withdrawn from trial during open-label phase	xx(xx.x)	xx / xx
Adverse event	xx(xx.x)	xx / xx
Death	xx(xx.x)	xx / xx
Lost to follow-up	xx(xx.x)	xx / xx
Withdrawal by subject	xx(xx.x)	xx / xx
Lack of efficacy	xx(xx.x)	xx / xx
Subject did not achieve treatment success after initial 4 weeks treatment	xx(xx.x)	xx / xx
Other	xx(xx.x)	xx / xx

N: Number of subjects, %: Percentage of subjects.

Shell 2: Disposition of subjects in the randomised phase: randomised subjects

	All randomised subjects (n=xxx)	LEO 90100 (n=xxx)	Vehicle (n=xxx)
	N (%)	N (%)	N (%)
Randomised subjects	xx (100.0)	xx (100.0)	xx (100.0)
Full analysis set	xx (xx.x)	xx (xx.x)	xx (xx.x)
Safety analysis set	xx (xx.x)	xx (xx.x)	xx (xx.x)
Per protocol analysis set	xx (xx.x)	xx (xx.x)	xx (xx.x)
Withdrawn from trial during randomised phase	xx (xx.x)	xx (xx.x)	xx (xx.x)
Adverse event	xx (xx.x)	xx (xx.x)	xx (xx.x)
Death	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lost to follow-up	xx (xx.x)	xx (xx.x)	xx (xx.x)
Withdrawal by subject	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lack of efficacy	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subject did not achieve treatment success after initial 4 weeks treatment[1]	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subject not clear or almost clear after treatment of relapse	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)

N: Number of subjects, %: Percentage of subjects.
1) Subjects randomised in error.

Shell 3: Reasons for leaving the trial during the open-label phase by last visit attended: enrolled subjects

	Open-label LEO 90100 (n=xxx)
Reason for withdrawal **Last visit attended**	**N (%)**
Adverse event	
Visit 1	xx(xx.x)
Visit 2	xx(xx.x)
Death	
Visit 1	xx(xx.x)
Visit 2	xx(xx.x)
Lost to follow-up	
Visit 1	xx(xx.x)
Visit 2	xx(xx.x)
Withdrawal by subject	
Visit 1	xx(xx.x)
Visit 2	xx(xx.x)
Lack of efficacy	
Visit 1	xx(xx.x)
Visit 2	xx(xx.x)
Subject did not achieve treatment success after initial 4 weeks treatment	
Visit 1	xx(xx.x)
Visit 2	xx(xx.x)
Other	
Visit 1	xx(xx.x)
Visit 2	xx(xx.x)

N: Number of subjects, %: Percentage of subjects.

Shell 4: Reasons for leaving the trial during the maintenance phase by last visit attended: randomised subjects

Reason for withdrawal Last visit attended	All randomised subjects (n=xxx) N (%)	LEO 90100 (n=xxx) N (%)	Vehicle (n=xxx) N (%)
Adverse event			
Visit 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 3	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 4	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 5	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 6	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 7	xx (xx.x)	xx (xx.x)	xx (xx.x)
...	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 15	xx (xx.x)	xx (xx.x)	xx (xx.x)
Death			
Visit 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 3	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 4	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 5	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 6	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 7	xx (xx.x)	xx (xx.x)	xx (xx.x)
...	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 15	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lost to follow-up			
<As above>			
...			
Subject did not achieve treatment success after initial 4 weeks treatment[1]			
<As above>			
...			
Other			
Visit 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 3	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 4	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 5	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 6	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 7	xx (xx.x)	xx (xx.x)	xx (xx.x)
...	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit 15	xx (xx.x)	xx (xx.x)	xx (xx.x)

N: Number of subjects, %: Percentage of subjects.
1) Subjects randomised in error.

Shell 5: <Continuous variable(s)>: open-label safety analysis set

	Open-label LEO 90100 (n=xxx)
<cont var 1>	
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x
...	
<cont var K>	
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile

Shell 6: <Continuous variable(s)>: randomised subjects

	All randomised subjects (n=xxx)	**LEO 90100 (n=xxx)**	**Vehicle (n=xxx)**
<cont var 1>			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
...			
<cont var K>			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile

Shell 7: <Continuous variable(s)> by <strata>: open-label safety analysis set

	Open-label LEO 90100 (n=xxx)
<cont var 1>	
<strata 1>	
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x
...	
<strata M>	
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x
...	
<cont var K>	
<strata 1>	
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x
...	
<strata M>	
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x

SD: Standard deviation, Q1: First quartile, Q3: Third quartile

Shell 8: <Continuous variable(s)> by <strata>: randomised subjects

	All randomised subjects (n=xxx)	**LEO 90100 (n=xxx)**	**Vehicle (n=xxx)**
<cont var 1>			
<strata 1>			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
...			
<strata M>			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
...			
<cont var K>			
<strata 1>			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
...			
<strata M>			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1: First quartile, Q3: Third quartile

Shell 9: <Categorical variable(s)>: open-label safety analysis set

	Open-label LEO 90100 (n=xxx)
<cat var 1>	
Number of subjects	xxx
Category 1	xxx (xx.x%)
...	xxx (xx.x%)
Category k_1	xxx (xx.x%)
...	
<cat var K>	
Number of subjects	xxx
Category 1	xxx (xx.x%)
...	xxx (xx.x%)
Category k_K	xxx (xx.x%)

Shell 10: <Categorical variable(s)>: randomised subjects

	All randomised subjects (n=xxx)	**LEO 90100 (n=xxx)**	**Vehicle (n=xxx)**
<cat var 1>			
Number of subjects	xxx	xxx	xxx
Category 1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
...	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Category k_1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
...			
<cat var K>			
Number of subjects	xxx	xxx	xxx
Category 1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
...	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Category k_K	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Shell 11: <Categorical variable(s)> by <strata>: open-label safety analysis set

	Open-label LEO 90100 (n=xxx)
<cat var 1>	
<strata 1>	
Number of subjects	xxx
Category 1	xxx (xx.x%)
...	xxx (xx.x%)
Category k_1	xxx (xx.x%)
...	
<strata M>	
Number of subjects	xxx
Category 1	xxx (xx.x%)
...	xxx (xx.x%)
Category k_1	xxx (xx.x%)
...	
<cat var K>	
<strata 1>	
Number of subjects	xxx
Category 1	xxx (xx.x%)
...	xxx (xx.x%)
Category k_K	xxx (xx.x%)
...	
<strata M>	
Number of subjects	xxx
Category 1	xxx (xx.x%)
...	xxx (xx.x%)
Category k_K	xxx (xx.x%)

Shell 12: <Categorical variable(s)> by <strata>: randomised subjects

	All randomised subjects (n=xxx)	**LEO 90100 (n=xxx)**	**Vehicle (n=xxx)**
<cat var 1>			
<strata 1>			
Number of subjects	xxx	xxx	xxx
Category 1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
...	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Category k_1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
...			
<strata M>			
Number of subjects	xxx	xxx	xxx
Category 1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
...	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Category k_M	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
...			
<cat var K>			
<strata 1>			
Number of subjects	xxx	xxx	xxx
Category 1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
...	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Category k_1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
...			
<strata M>			
Number of subjects	xxx	xxx	xxx
Category 1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
...	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Category k_M	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Shell 13: Location of psoriasis and location of other psoriasis at baseline: open-label safety analysis set

	Open-label LEO 90100 (n=xxx)
Location of psoriasis	
Number of subjects	xxx
Abdomen	xxx (xx.x%)
Chest	xxx (xx.x%)
Elbow	xxx (xx.x%)
Forearm incl. hand	xxx (xx.x%)
Knee	xxx (xx.x%)
Lower back	xxx (xx.x%)
Lower leg incl. foot	xxx (xx.x%)
Neck	xxx (xx.x%)
Upper arm	xxx (xx.x%)
Upper back	xxx (xx.x%)
Upper leg	xxx (xx.x%)
Location of other psoriasis	
Number of subjects	xxx
Face	xxx (xx.x%)
Genitals	xxx (xx.x%)
Nails	xxx (xx.x%)
Palms	xxx (xx.x%)
Scalp	xxx (xx.x%)
Skin folds	xxx (xx.x%)
Soles	xxx (xx.x%)

Shell 14: Location of psoriasis and location of other psoriasis at baseline: randomised subjects

	All randomised subjects (n=xxx)	**LEO 90100 (n=xxx)**	**Vehicle (n=xxx)**
Location of psoriasis			
Number of subjects	xxx	xxx	xxx
Abdomen	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Chest	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Elbow	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Forearm incl. hand	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Knee	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Lower back	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Lower leg incl. foot	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Neck	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Upper arm	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Upper back	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Upper leg	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Location of other psoriasis			
Number of subjects	Xxx	xxx	xxx
Face	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Genitals	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Nails	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Palms	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Scalp	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Skin folds	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Soles	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Subjects may appear in more than one category.

Shell 15: Concomitant medication: open-label safety analysis set

Medication (ATC code)	Open-label LEO 90100 (n=xxx) Number of subjects (%)
ACT1	xx(xx.x)
ACT2	xx(xx.x)
ACT3	xx(xx.x)
ACT4	xx(xx.x)
Preferred drug name	xx(xx.x)
...	

ATC: Anatomical Therapeutic Chemical Classification System.

Shell 16: Concomitant medication: randomised subjects

Medication (ATC code)	All randomised subjects (n=xxx) Number of subjects (%)	LEO 90100 (n=xxx) Number of subjects (%)	Vehicle (n=xxx) Number of subjects (%)
ACT1	xx(xx.x)	xx(xx.x)	xx(xx.x)
ACT2	xx(xx.x)	xx(xx.x)	xx(xx.x)
ACT3	xx(xx.x)	xx(xx.x)	xx(xx.x)
ACT4	xx(xx.x)	xx(xx.x)	xx(xx.x)
Preferred drug name	xx(xx.x)	xx(xx.x)	xx(xx.x)
...			

ATC: Anatomical Therapeutic Chemical Classification System.

Shell 17: Previous and latest systemic anti-psoriatic treatment: open-label safety analysis set

	Open-label LEO 90100 (n=xxx)
Previous systemic anti-psoriatic treatment	
Number of subjects	xxx
Acitretin	xxx (xx.x%)
Adalimumab	xxx (xx.x%)
Apremilast	xxx (xx.x%)
Cyclosporin	xxx (xx.x%)
Etanercept	xxx (xx.x%)
Infliximab	xxx (xx.x%)
Methotrexate	xxx (xx.x%)
Phototherapy	xxx (xx.x%)
Secukinumab	xxx (xx.x%)
Ustekinumab	xxx (xx.x%)
Other	xxx (xx.x%)
Latest systemic anti-psoriatic treatment	
Number of subjects	xxx
Acitretin	xxx (xx.x%)
Adalimumab	xxx (xx.x%)
Apremilast	xxx (xx.x%)
Cyclosporin	xxx (xx.x%)
Etanercept	xxx (xx.x%)
Infliximab	xxx (xx.x%)
Methotrexate	xxx (xx.x%)
Phototherapy	xxx (xx.x%)
Secukinumab	xxx (xx.x%)
Ustekinumab	xxx (xx.x%)
Other	xxx (xx.x%)

Subjects may appear in more than one category.

Shell 18: Previous and latest systemic anti-psoriatic treatment: randomised subjects

	All randomised subjects (n=xxx)	**LEO 90100 (n=xxx)**	**Vehicle (n=xxx)**
Previous systemic anti-psoriatic treatment			
Number of subjects	xxx	xxx	xxx
Acitretin	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Adalimumab	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Apremilast	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Cyclosporin	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Etanercept	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Infliximab	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Methotrexate	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Phototherapy	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Secukinumab	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Ustekinumab	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Other	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Latest systemic anti-psoriatic treatment			
Number of subjects	xxx	xxx	xxx
Acitretin	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Adalimumab	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Apremilast	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Cyclosporin	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Etanercept	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Infliximab	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Methotrexate	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Phototherapy	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Secukinumab	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Ustekinumab	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Other	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Subjects may appear in more than one category.

Shell 19: Concurrent diagnoses at baseline: open-label safety analysis set

System Organ Class (SOC) Preferred term	Open-label LEO 90100 (n=xxx) N (%)
Total number of diagnoses	xxx
Number of subjects with a diagnosis	xxx
SOC 1	xxx(xx.x)
Preferred term 1	xxx(xx.x)
...	...
Preferred term k_1	xxx(xx.x)
SOC 2	xxx(xx.x)
Preferred term 1	xxx(xx.x)
...	...
Preferred term k_2	xxx(xx.x)
...	
SOC M	xxx(xx.x)
Preferred term 1	xxx(xx.x)
...	...
Preferred term k_M	xxx(xx.x)

Shell 20: Summary of observation types for time to first relapse – sensitivity analysis: <full analysis set / per protocol analysis set>

	LEO 90100 (n=xxx) Subjects (%)	**Vehicle (n=xxx) Subjects (%)**
Number of subjects with:		
No relapses[1]	xxx (xx.x%)	xxx (xx.x%)
Relapse confirmed at a scheduled visit[2]	xxx (xx.x%)	xxx (xx.x%)
Relapse confirmed at an unscheduled visit[3]	xxx (xx.x%)	xxx (xx.x%)
Total	xxx (100.0%)	xxx (100.0%)

1) No relapses corresponds to right-censored observations.
2) Relapse confirmed at a scheduled visit corresponds to interval censored observations.
3) Relapse confirmed at an unscheduled visit corresponds to exact observations.

Shell 21: Censored and uncensored observations for time to first relapse: <full analysis set / per protocol analysis set>

	LEO 90100 (n=xxx) Subjects (%)	**Vehicle (n=xxx) Subjects (%)**
Number of subjects with:		
No relapses[1]	xxx (xx.x%)	xxx (xx.x%)
Relapses confirmed[2]	xxx (xx.x%)	xxx (xx.x%)
Total	xxx (100.0%)	xxx (100.0%)

1) No relapses corresponds to censored observations.
2) Relapses confirmed correspond to uncensored observations.

Shell 22: Number of subjects at risk of first relapse by scheduled visit: <full analysis set / per protocol analysis set>

Time relative to randomisation	LEO 90100 (n=xxx) Subjects (%[1])	Vehicle (n=xxx) Subjects (%[1])
Randomisation, Visit 2		
Number of subjects attending the visit	xxx	xxx
Number of subjects still at risk of first relapse	xxx (xx.x%)	xxx (xx.x%)
28 days[2], Visit 3		
Number of subjects attending the visit	xxx	xxx
Number of subjects still at risk of first relapse	xxx (xx.x%)	xxx (xx.x%)
...		
364 days[2], Visit 15		
Number of subjects attending the visit	xxx	xxx
Number of subjects still at risk of first relapse	xxx (xx.x%)	xxx (xx.x%)

1) Percents are calculated as number of subjects still at risk of first relapse divided by number of subjects in the <full analysis set / per protocol analysis set> multiplied by 100.
2) Number of days since randomisation assuming the scheduled visits happen every fourth week.

Shell 23:< Statistical/Sensitivity> analysis of time to first relapse: <full analysis set / per protocol analysis set>

	LEO 90100 vs. vehicle
Number of subjects randomised to LEO 90100	xxx
Number of subjects randomised to Vehicle	xxx
Hazard ratio	xx.xx
95% CI	xx.xx-xx.xx
p-value	0.xxx or <0.001

Estimates are obtained from a proportional hazards model with treatment group, pooled sites, and disease severity at maintenance baseline (determined by PGA) as factors. <The model incorporates interval censoring>.

Shell 24: Percentiles from estimated survival curves < - sensitivity analysis>: <full analysis set / per protocol analysis set>

Percentiles **Estimated number of days after randomisation**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
25%		
Estimate	xxx	xxx
95% CI	xxx-xxx	xxx-xxx
50%		
Estimate	xxx	xxx
95% CI	xxx-xxx	xxx-xxx
75%		
Estimate	xxx	xxx
95% CI	xxx-xxx	xxx-xxx

The percentiles are obtained from the estimated survival curves. The percentiles describe the number of days after randomisation until a certain percent of subjects are no longer at risk.
<The survival curves are estimated using a non-parametric maximum likelihood estimator, namely the Turnbull self-consistency algorithm.>

Shell 25: Comparison of proportions of subjects still at risk of first relapse at 26 weeks and 52 weeks after randomisation: full analysis set

Weeks after randomisation **Proportion of subjects**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**	**p-value[1]**
26 weeks			
Estimate	xx.xx	xx.xx	0.xxx or <0.001
95% CI	xx.xx-xx.xx	xx.xx-xx.xx	
52 weeks			
Estimate	xx.xx	xx.xx	0.xxx or <0.001
95% CI	xx.xx-xx.xx	xx.xx-xx.xx	

The proportion are obtained from the estimated survival curves.

1) The p-value is obtained from a z-test comparing LEO 90100 to vehicle.

Shell 26: Observed proportion of days in remission: <full analysis set / per protocol analysis set>

Proportion of days in remission	**LEO 90100 (n=xxx)**	**Vehicle (n=xxx)**
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile

Shell 27: <Statistical / Sensitivity> analysis of proportion of days in remission: <full analysis set / per protocol analysis set>

	LEO 90100 vs. vehicle
Number of subjects randomised to LEO 90100	xxx
Number of subjects randomised to vehicle	xxx
Treatment difference	xx.xx
95% CI	xx.xx-xx.xx
p-value	0.xxx or <0.001

Estimates are obtained using multiple imputation with 100 imputation and an ANOVA model with treatment group, pooled trial site, and disease severity at maintenance baseline as factors. Estimates are pooled using Rubin's rule to draw inference.

Shell 28: Number of relapses during maintenance phase: <full analysis set / per protocol analysis set>

	LEO 90100 (n=xxx)	**Vehicle (n=xxx)**
PYE	xxx.x	xxx.x
Number of subjects	xxx	xxx
Mean(SD)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx;xx	xx;xx
Total number of relapses	xxx	xxx
Rate	xx.x	xx.x

PYE: Patient years of exposure, SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile, Rate: Number of relapses divided by patient years of exposure multiplied by 100.

Shell 29: <Statistical / Sensitivity> analysis of number of relapses during maintenance phase <(negative binomial model)>: <full analysis set / per protocol analysis set>

	LEO 90100 vs. Vehicle
Number of subjects randomised to LEO 90100	xxx
Number of subjects randomised to Vehicle	xxx
Rate ratio	xx.xx
95% CI	xx.xx-xx.xx
p-value	0.xxx or <0.001

Estimates are obtained from a <Poisson regression model/negative binomial model> with treatment group, pooled site, and disease severity at maintenance baseline (determined by PGA) as factors, subject as random effect, and risk time as an offset.

Shell 30: <xxx> by visit in open-label phase: open-label safety analysis set

Visit <xxx>	Open-label safety analysis set (n=xxx)	Randomised subjects (n=xxx)	Not randomised subjects (n=xxx)
Visit 1			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Visit 2			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile

Shell 31: <Change / Percent change> in <xxx> from start to end of open-label phase: open-label safety analysis set

<Change / Percent change> from visit 1 to visit 2	Open-label safety analysis set (n=xxx)	Randomised subjects (n=xxx)	Not randomised subjects (n=xxx)
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile

Shell 32: <xxx> by visit not related to relapse: full analysis set

Visit <xxx>	LEO 90100 (n=xxx)	Vehicle (n=xxx)
Visit 2		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
Visit 3		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
...		
Visit 15		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile

Shell 33: <xxx> by visit for start of relapse: full analysis set

Visit interval **<xxx>**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
Visit 2-visit 3		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
Visit 3		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
Visit 3-visit 4		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
Visit 4		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
...		
Visit 14-visit 15		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
Total		
Number of relapses	xxx	xxx
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile

Shell 34: <xxx> by visit for end of relapse: full analysis set

Visit interval **<xxx>**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
Visit 3-visit 4		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
Visit 4		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
Visit 4-visit 5		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
...		
Visit 15		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
Visit 15-visit X		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
Total		
Number of relapses	xxx	xxx
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile

Shell 35: <Change / Percent change> in <xxx> from start of relapse to end of relapse by visit for start of relapse: full analysis set

Visit interval **<Change / Percent change> in <xxx>** **from start to end of relapse period**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
Visit 2-visit 3		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
Visit 3		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
Visit 3-visit 4		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
...		
Visit 14-visit 15		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
Total		
Number of relapses	xxx	xxx
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile

Shell 36: <Physician's / Subject's> global assessment of disease severity by visit in open-label phase: open-label safety analysis set

Visit **<Physician's / Subject's> Global Assessment of Disease Severity**	**Open-label safety analysis set (n=xxx)**	**Randomised subjects (n=xxx)**	**Not randomised subjects (n=xxx)**
Visit 1			
Number of subjects	xxx	xxx	xxx
Clear	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
<Almost clear/Very mild>	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Visit 2			
Number of subjects	xxx	xxx	xxx
Clear	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
<Almost clear/Very mild>	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Shell 37: Shift table for <physician's / subject's> global assessment of disease severity from start to end of open-label phase: open-label safety analysis set

	Open-label safety analysis set (n=xxx)					Randomised subjects (n=xxx)					Not randomised subjects (n=xxx)				
Visit	**Visit 2**					**Visit 2**					**Visit 2**				
<Physician's / Subject's> Global Assessment of Disease Severity	**Clear**	**<AC/VM>**	**Mild**	**Mod**	**Sev**	**Clear**	**<AC/VM>**	**Mild**	**Mod**	**Sev**	**Clear**	**<AC/VM>**	**Mild**	**Mod**	**Sev**
Visit 1															
Clear	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
<Almost clear/Very mild>	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

<AC: Almost clear/VM: Very mild>, Mod: Moderate, Sev: Severe

Shell 38: <Physician's / Subject's> Global Assessment of Disease Severity by visit not related to relapse: full analysis set

Visit **<Physician's / Subject's> Global Assessment of Disease Severity**	**LEO 90100 (n=xxx)**	**Vehicle (n=xxx)**
Visit 2		
Number of subjects	xxx	xxx
Clear	xxx (xx.x%)	xxx (xx.x%)
<Almost clear/Very mild>	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
...		
Visit 15		
Number of subjects	xxx	xxx
Clear	xxx (xx.x%)	xxx (xx.x%)
<Almost clear/Very mild>	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)

Shell 39: <Physician's / Subject's> global assessment of disease severity by visit for start of relapse: full analysis set

Visit **<Physician's / Subject's> Global Assessment of Disease Severity**	**LEO 90100 (n=xxx)**	**Vehicle (n=xxx)**
Visit 2-visit 3		
Number of subjects	xxx	xxx
Clear	xxx (xx.x%)	xxx (xx.x%)
<Almost clear/Very mild>	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Visit 3		
Number of subjects	xxx	xxx
Clear	xxx (xx.x%)	xxx (xx.x%)
<Almost clear/Very mild>	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Visit 3-visit 4		
Number of subjects	xxx	xxx
Clear	xxx (xx.x%)	xxx (xx.x%)
<Almost clear/Very mild>	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
...		
Visit 14-visit 15		
Number of subjects	xxx	xxx
Clear	xxx (xx.x%)	xxx (xx.x%)
<Almost clear/Very mild>	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Total		
Number of relapses	xxx	xxx
Number of subjects	xxx	xxx
Clear	xxx (xx.x%)	xxx (xx.x%)
<Almost clear/Very mild>	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)

Shell 40: <Physician's / Subject's> global assessment of disease severity by visit for end of relapse: full analysis set

Visit **<Physician's / Subject's> Global Assessment of Disease Severity**	**LEO 90100 (n=xxx)**	**Vehicle (n=xxx)**
Visit 3-visit 4		
Number of subjects	xxx	xxx
Clear	xxx (xx.x%)	xxx (xx.x%)
<Almost clear/Very mild>	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Visit 4		
Number of subjects	xxx	xxx
Clear	xxx (xx.x%)	xxx (xx.x%)
<Almost clear/Very mild>	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Visit 4-visit 5		
Number of subjects	xxx	xxx
Clear	xxx (xx.x%)	xxx (xx.x%)
<Almost clear/Very mild>	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
...		
Visit 15		
Number of subjects	xxx	xxx
Clear	xxx (xx.x%)	xxx (xx.x%)
<Almost clear/Very mild>	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Visit 15-UNS[1]		
Number of subjects	xxx	xxx
Clear	xxx (xx.x%)	xxx (xx.x%)
<Almost clear/Very mild>	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Total		
Number of relapses	xxx	xxx
Number of subjects	xxx	xxx
Clear	xxx (xx.x%)	xxx (xx.x%)
<Almost clear/Very mild>	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)

1) Possible unscheduled visits (UNS) in the maintenance phase after visit 15.

Shell 41: Shift table for <physician's / subject's> global assessment of disease severity from start of relapse to end of relapse by visit for start of relapse: full analysis set

	LEO 90100 (n=xxx)					Vehicle (n=xxx)				
	End of relapse					End of relapse				
Visit for start of relapse <Physician's / Subject's> Global Assessment of Disease Severity	**Clear**	**<AC/VM>**	**Mild**	**Mod**	**Sev**	**Clear**	**<AC/VM>**	**Mild**	**Mod**	**Sev**
Visit 2-visit 3										
Clear	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
<Almost clear/Very mild>	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Visit 3										
Clear	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
<Almost clear/Very mild>	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Visit 3-visit 4										
Clear	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
<Almost clear/Very mild>	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
...										

continued...

	LEO 90100 (n=xxx)					Vehicle (n=xxx)				
	End of relapse					End of relapse				
Visit for start of relapse <Physician's / Subject's> Global Assessment of Disease Severity	**Clear**	**<AC/VM>**	**Mild**	**Mod**	**Sev**	**Clear**	**<AC/VM>**	**Mild**	**Mod**	**Sev**
Visit 14-visit 15										
Clear	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
<Almost clear/Very mild>	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Total										
Clear	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
<Almost clear/Very mild>	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

<AC: Almost clear/VM: Very mild>, Mod: Moderate, Sev: Severe

Shell 42: WPAI:PSO by visit: full analysis set

	LEO 90100			Vehicle		
Visit **WPAI:PSO Score**	**Total**	**In remission at visit**	**In relapse at visit**	**Total**	**In remission at visit**	**In relapse at visit**
Visit 2						
Current work status						
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
No	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Absenteeism						
N	xxx	xxx	xxx	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x(xx.x)	xx.x(xx.x)	xx.x (xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Presenteeism						
N	xxx	xxx	xxx	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x(xx.x)	xx.x(xx.x)	xx.x (xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x

continued…

	LEO 90100			Vehicle		
	Total	**In remission at visit**	**In relapse at visit**	**Total**	**In remission at visit**	**In relapse at visit**
Visit **WPAI:PSO Score**						
TWPI						
N	xxx	xxx	xxx	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x(xx.x)	xx.x(xx.x)	xx.x (xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
TAI						
N	xxx	xxx	xxx	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x(xx.x)	xx.x(xx.x)	xx.x (xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Visit 8						
<as above>						
Visit 15						
<as above>						

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile, TWPI: Total work productivity impairment, TAI: Total activity impairment.
Subjects are included in the relapse category in each treatment group if they have been on rescue medication during the past 7 days up to the visit.

Shell 43: WPAI:PSO by visit: open-label safety analysis set

Visit WPAI:PSO Score	Open-label safety analysis set (n=xxx)	Randomised subjects (n=xxx)	Not randomised subjects (n=xxx)
Visit 1			
Current work status			
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
No	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Absenteeism			
N	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Presenteeism			
N	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
TWPI			
N	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x

continued…

Visit **WPAI:PSO Score**	**Open-label safety analysis set (n=xxx)**	**Randomised subjects (n=xxx)**	**Not randomised subjects (n=xxx)**
TAI			
N	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Visit 2			
<as above>			

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile, TWPI: Total work productivity impairment, TAI: Total activity impairment.

Shell 44: Total PSI score during open-label phase; open-label safety analysis set.

Total PSI score (AUC)	**Open-label safety analysis set (n=xxx)**	**Randomised subjects (n=xxx)**	**Not randomised subjects (n=xxx)**
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile, AUC: Area under the curve. AUC is calculated based on all the daily total PSI scores using the trapezoidal rule to approximate the area under and is normalised by the total number of days in the open-label phase.

Shell 45: <Change / Percent change> in total PSI score from start to end of open-label phase: open-label safety analysis set

Total PSI score from visit 1 to visit 2	**Open-label safety analysis set (n=xxx)**	**Randomised subjects (n=xxx)**	**Not randomised subjects (n=xxx)**
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile

Shell 46: Total PSI score for time on rescue medication and time in remission during the first 28 weeks of the maintenance phase: full analysis set

Total PSI score (AUC)	LEO 90100 (n=xxx)	Vehicle (n=xxx)
Time in remission		
Number of subjects	xxx	xxx
Mean (SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
Time in relapse		
Number of subjects	xxx	xxx
Mean (SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
Time in maintenance phase		
Number of subjects	xxx	xxx
Mean (SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1:1st quartile, Q3: 3rd quartile, AUC: Area under the curve.
Average PSI score is calculated as area under the curve (AUC) over the time intervals on rescue medication and the time intervals in remission for each subject. AUC is calculated based on all the weekly total PSI scores using the trapezoidal rule to approximate the area under and is normalised by the total number of days remission or relapse, respectively.

Shell 47: Statistical analysis of PSI: full analysis set

Weeks from randomisation	**LEO 90100 vs. vehicle**
Number of subjects randomised to LEO 90100	xxx
Number of subjects randomised to vehicle	xxx
Randomisation	
Estimated means	
LEO 90100	xx.xx
Vehicle	xx.xx
Treatment difference	xx.xx
95% CI	xx.xx-xx.xx
p-value	0.xxx or <0.001
Week 4	
Estimated means	
LEO 90100	
Vehicle	
Treatment difference	
95% CI	
p-value	
...	

continued…

Weeks from randomisation	**LEO 90100 vs. vehicle**
Week 28 Estimated means LEO 90100 Vehicle Treatment difference 95% CI p-value	

Estimates are obtained from a Mixed effect Model Repeat Measurement (MMRM) including treatment group, days from randomisation, interaction between treatment and time, relapse status, PSI total score at time of randomisation. Multiple imputation is used to impute missing assessment of PSI. Rubin's rule is used to pool the estimates for the inference.

Shell 48: Statistical analysis of DLQI: full analysis set

	LEO 90100 vs. vehicle
Number of subjects randomised to LEO 90100	xxx
Number of subjects randomised to vehicle	xxx
Visit 2	
Estimated means	
LEO 90100	xx.xx
Vehicle	xx.xx
Treatment difference	xx.xx
95% CI	xx.xx-xx.xx
p-value	0.xxx or <0.001
...	
Visit 15	
Estimated means	
LEO 90100	
Vehicle	
Treatment difference	
95% CI	
p-value	

Estimates are obtained from a Mixed effect Model Repeat measurement (MMRM) including treatment group, days from randomisation, interaction between treatment and time, relapse status, DLQI total score at time of randomisation. Multiple imputation is used to impute missing assessment of DLQI. Rubin's rule is used to pool the estimates for the inference.

Shell 49: Shift table for EQ-5D-5L from start to end of open-label phase: open-label safety analysis set

	Open-label safety analysis set (n=xxx)					Randomised subjects (n=xxx)					Not randomised subjects (n=xxx)				
Visit	Visit 2					Visit 2					Visit 2				
EQ-5D-5L	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4
Visit 1															
Mobility															
0: I have no problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I have slight problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I have moderate problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I am unable to walk	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Self-care															
0: I have no problems washing or dressing myself	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I have slight washing or dressing myself	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I have moderate washing or dressing myself	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe washing or dressing myself	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I am unable to wash or dress myself	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Usual activities															
0: I have no problems doing my usual activities	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I have slight problems doing my usual activities	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I have moderate problems doing my usual activities	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe problems doing my usual activities	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I am unable to do my usual activities	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

continued…

Visit EQ-5D-5L	Open-label safety analysis set (n=xxx) Visit 2 0 1 2 3 4	Randomised subjects (n=xxx) Visit 2 0 1 2 3 4	Not randomised subjects (n=xxx) Visit 2 0 1 2 3 4
Pain/discomfort			
0: I have no pain or discomfort	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
1: I have slight pain or discomfort	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
2: I have moderate pain or discomfort	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
3: I have severe pain or discomfort	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
4: I have extreme pain or discomfort	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
Anxiety/depression			
0: I am not anxious or depressed	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
1: I am slightly anxious or depressed	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
2: I am moderate problems walking	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
3: I have severe problems walking	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
4: I am unable to walk	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
Skin irritation			
0: I have no itching	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
1: I have slight itching	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
2: I have moderate itching	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
3: I have severe itching	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
4: I have extreme itching	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
Self-confidence			
0: I have no problems with self-confidence	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
1: I have slight problems with self-confidence	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
2: I have moderate problems with self-confidence	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
3: I have severe problems with self-confidence	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx
4: I have extreme problems with self-confidence	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx	xxx xxx xxx xxx xxx

Column numbers refers to the numbering in each question.

Shell 50: Shift table for EQ-5D-5L-PSO dimensions from start of relapse to end of relapse by visit for start of relapse: maintenance full analysis set

	LEO 90100 (n=xxx)					Vehicle (n=xxx)				
	End of relapse					End of relapse				
Visit EQ-5D-5L	0	1	2	3	4	0	1	2	3	4
Visit 2-visit 3										
Mobility										
0: I have no problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I have slight problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I have moderate problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I am unable to walk	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Self-care										
0: I have no problems washing or dressing myself	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I have slight washing or dressing myself	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I have moderate washing or dressing myself	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe washing or dressing myself	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I am unable to wash or dress myself	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Usual activities										
0: I have no problems doing my usual activities	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I have slight problems doing my usual activities	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I have moderate problems doing my usual activities	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe problems doing my usual activities	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I am unable to do my usual activities	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

continued...

	LEO 90100 (n=xxx)					Vehicle (n=xxx)				
	End of relapse					End of relapse				
Visit **EQ-5D-5L**	**0**	**1**	**2**	**3**	**4**	**0**	**1**	**2**	**3**	**4**
Pain/discomfort										
0: I have no pain or discomfort	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I have slight pain or discomfort	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I have moderate pain or discomfort	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe pain or discomfort	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I have extreme pain or discomfort	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Anxiety/depression										
0: I am not anxious or depressed	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I am slightly anxious or depressed	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I am moderate problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I am unable to walk	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Skin irritation										
0: I have no itching	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I have slight itching	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I have moderate itching	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe itching	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I have extreme itching	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Self-confidence										
0: I have no problems with self-confidence	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I have slight problems with self-confidence	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I have moderate problems with self-confidence	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe problems with self-confidence	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I have extreme problems with self-confidence	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

continued...

	LEO 90100 (n=xxx)					Vehicle (n=xxx)				
	End of relapse					End of relapse				
Visit **EQ-5D-5L**	**0**	**1**	**2**	**3**	**4**	**0**	**1**	**2**	**3**	**4**
Visit 3										
.										
.										
Visit 3-visit 4										
.										
.										
Visit 15 – UNS[1]										
.										
.										
Total										
Mobility										
0: I have no problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I have slight problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I have moderate problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I am unable to walk	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

continued…

Visit EQ-5D-5L	LEO 90100 (n=xxx) End of relapse 0	1	2	3	4	Vehicle (n=xxx) End of relapse 0	1	2	3	4
Self-care										
0: I have no problems washing or dressing myself	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I have slight washing or dressing myself	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I have moderate washing or dressing myself	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe washing or dressing myself	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I am unable to wash or dress myself	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Usual activities										
0: I have no problems doing my usual activities	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I have slight problems doing my usual activities	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I have moderate problems doing my usual activities	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe problems doing my usual activities	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I am unable to do my usual activities	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Pain/discomfort										
0: I have no pain or discomfort	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I have slight pain or discomfort	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I have moderate pain or discomfort	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe pain or discomfort	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I have extreme pain or discomfort	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Anxiety/depression										
0: I am not anxious or depressed	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I am slightly anxious or depressed	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I am moderate problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe problems walking	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I am unable to walk	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

continued...

Visit EQ-5D-5L	LEO 90100 (n=xxx) End of relapse 0	1	2	3	4	Vehicle (n=xxx) End of relapse 0	1	2	3	4
Skin irritation										
0: I have no itching	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I have slight itching	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I have moderate itching	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe itching	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I have extreme itching	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Self-confidence										
0: I have no problems with self-confidence	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
1: I have slight problems with self-confidence	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
2: I have moderate problems with self-confidence	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3: I have severe problems with self-confidence	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4: I have extreme problems with self-confidence	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Column numbers refers to the numbering in each question.
1)Possible unscheduled visits (UNS) in the maintenance phase after visit 15.

Shell 51: Subjects in remission by scheduled visit: full analysis set

Visit	**LEO 90100 (n=xxx)**	**Vehicle (n=xxx)**
Visit 2		
Number of subjects attending the visit	xxx	xxx
Number of subjects in remission	xxx (xx.x%)	xxx (xx.x%)
Visit 3		
<as above>		
...		
Visit 15		
<as above>		

Shell 52: Subjects achieving clear or almost clear after treatment of relapse by number of relapses: full analysis set

Number of relapses	LEO 90100 (n=xxx)	Vehicle (n=xxx)
1st		
Number of subjects with relapse	xxx	xxx
Number of subjects achieving clear or almost clear	xxx (xx.x%)	xxx (xx.x%)
2nd		
<as above>		
3rd		
<as above>		
4th		
<as above>		
5th		
<as above>		
6th		
<as above>		
7th		
<as above>		
8th		
<as above>		

Shell 53: Target lesion/location score by visit in open-label phase: open-label safety analysis set

Target lesion/location score Visit	Open-label safety analysis set (n=xxx)	Randomised subjects (n=xxx)	Not randomised subjects (n=xxx)
Redness			
Visit 1			
Number of subjects	xxx	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Visit 2			
<as above>			
Thickness			
Visit 1			
Number of subjects	xxx	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Visit 2			
<as above>			
Scaliness			
Visit 1			
Number of subjects	xxx	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Visit 2			
<as above>			

Shell 54: Shift table for target lesion/location score from start to end of open-label phase: open-label safety analysis set

	Open-label safety analysis set (n=xxx)					Randomised subjects (n=xxx)					Not randomised subjects (n=xxx)				
	Visit 2					Visit 2					Visit 2				
Visit **Target lesion/location score**	**None**	**Mild**	**Mod**	**Sev**	**VS**	**None**	**Mild**	**Mod**	**Sev**	**VS**	**None**	**Mild**	**Mod**	**Sev**	**VS**
Visit 1															
Redness															
None	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Very severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Thickness															
None	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Very severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Scaliness															
None	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Very severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Mod: Moderate, Sev: Severe, VS: Very severe

Shell 55: Target lesion/location score by visit not related to relapse: full analysis set

Target lesion/location score **Visit**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
Redness		
Visit 2		
Number of subjects	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)
...		
Visit 15		
<as above>		
Thickness		
Visit 2		
Number of subjects	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)
...		
Visit 15		
<as above>		
Scaliness		
Visit 2		
Number of subjects	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)
...		
Visit 15		
<as above>		

Shell 56: Target lesion/location score by visit for start of relapse: full analysis set

Target lesion/location score **Visit**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
Redness		
Visit 2-visit 3		
Number of subjects	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)
Visit 3		
<as above>		
Visit 3-visit 4		
<as above>		
...		
Visit 14-visit 15		
<as above>		
Total		
Number of relapses	xxx	xxx
Number of subjects	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)
Thickness		
Visit 2-visit 3		
Number of subjects	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)
Visit 3		
<as above>		
Visit 3-visit 4		
<as above>		
...		
Visit 14-visit 15		
<as above>		

continued…

Target lesion/location score **Visit**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
Total		
Number of relapses	xxx	xxx
Number of subjects	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)
Scaliness		
Visit 2-visit 3		
Number of subjects	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)
Visit 3		
<as above>		
Visit 3-visit 4		
<as above>		
...		
Visit 14-visit 15		
<as above>		
Total		
Number of relapses	xxx	xxx
Number of subjects	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)

Shell 57: Target lesion/location score by visit for end of relapse: full analysis set

Target lesion/location score **Visit**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
Redness		
Visit 3-visit 4		
Number of subjects	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)
Visit 4		
<as above>		
Visit 4-visit 5		
<as above>		
...		
Visit 15		
<as above>		
Visit 15-UNS[1]		
<as above>		
Total		
Number of relapses	xxx	xxx
Number of subjects	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)
Thickness		
Visit 3-visit 4		
Number of subjects	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)
Visit 4		
<as above>		
Visit 4-visit 5		
<as above>		
...		
Visit 15		
<as above>		
Visit 15-UNS[1]		
<as above>		

continued…

Target lesion/location score **Visit**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
Total		
Number of relapses	xxx	xxx
Number of subjects	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)
Scaliness		
Visit 3-visit 4		
Number of subjects	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)
Visit 4		
<as above>		
Visit 4-visit 5		
<as above>		
...		
Visit 15		
<as above>		
Visit 15-UNS[1]		
<as above>		
Total		
Number of relapses	xxx	xxx
Number of subjects	xxx	xxx
None	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Very severe	xxx (xx.x%)	xxx (xx.x%)

Shell 58: Shift table for target lesion/location score from start of relapse to end of relapse by visit for start of relapse: full analysis set

	LEO 90100 (n=xxx)					Vehicle (n=xxx)				
	End of relapse					End of relapse				
Target lesion/location score Visit interval	None	Mild	Mod	Sev	VS	None	Mild	Mod	Sev	VS
Redness										
Visit 2-visit 3										
None	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Very severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Visit 3										
None	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Very severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Visit 3-visit 4										
None	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Very severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

...

continued….

	LEO 90100 (n=xxx)					Vehicle (n=xxx)				
	End of relapse					End of relapse				
Target lesion/location score **Visit interval**	**None**	**Mild**	**Mod**	**Sev**	**VS**	**None**	**Mild**	**Mod**	**Sev**	**VS**
Visit 14-visit 15										
None	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Very severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Total										
None	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Very severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Thickness										
<as above>										
Scaliness										
<as above>										

Mod: Moderate, Sev: Severe, VS: Very severe

Shell 59: Overall summary of adverse events during open-label phase: open-label safety analysis set

	Open-label LEO 90100 (n=xxx)			
	N	**(%)**	**E**	**R**
PYE	xxx.xx			
Events	xxx	(xx.x)	xxx	xxx.x
Serious	xxx	(xx.x)	xxx	xxx.x
Severity				
Mild	xxx	(xx.x)	xxx	xxx.x
Moderate	xxx	(xx.x)	xxx	xxx.x
Severe	xxx	(xx.x)	xxx	xxx.x
Related[1] to IMP	xxx	(xx.x)	xxx	xxx.x
Leading to withdrawal from trial	xxx	(xx.x)	xxx	xxx.x
Action taken with IMP				
Dose not changed	xxx	(xx.x)	xxx	xxx.x
Dose reduced	xxx	(xx.x)	xxx	xxx.x
Dose increased	xxx	(xx.x)	xxx	xxx.x
Drug interrupted	xxx	(xx.x)	xxx	xxx.x
Drug withdrawn	xxx	(xx.x)	xxx	xxx.x
Not applicable	xxx	(xx.x)	xxx	xxx.x
Unknown	xxx	(xx.x)	xxx	xxx.x
Outcome				
Fatal	xxx	(xx.x)	xxx	xxx.x
Not recovered/Not resolved	xxx	(xx.x)	xxx	xxx.x
Recovering/Resolving	xxx	(xx.x)	xxx	xxx.x
Recovered/Resolved	xxx	(xx.x)	xxx	xxx.x
Recovered/Resolved with sequelae	xxx	(xx.x)	xxx	xxx.x
Unknown	xxx	(xx.x)	xxx	xxx.x

AEs collected during the exposure time in the initial open-label phase are shown.
IMP: Investigational medicinal product, PYE: Patient years of exposure, N: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of adverse events, R: Rate (number of adverse events divided by patient years of exposure multiplied by 100).
1) Considered possibly or probably related to trial product by the investigator.

Shell 60: Overall summary of adverse events during <XXX> by randomised treatment: safety analysis set

	LEO 90100 (n=xxx)				Vehicle (n=xxx)			
	N	**(%)**	**E**	**R**	**N**	**(%)**	**E**	**R**
PYE	xxx.xx				xxx.xx			
Events	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Serious	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Severity								
Mild	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Moderate	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Severe	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Related[1] to IMP	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Leading to withdrawal from trial	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Action taken with IMP								
Dose not changed	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Dose reduced	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Dose increased	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Drug interrupted	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Drug withdrawn	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Not applicable	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Unknown	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Outcome								
Fatal	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Not recovered/Not resolved	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Recovering/Resolving	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Recovered/Resolved	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Recovered/Resolved with sequelae	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x
Unknown	xxx	(xx.x)	xxx	xxx.x	xxx	(xx.x)	xxx	xxx.x

AEs collected during the exposure time in the <total/first 28 weeks of the/remaining 24 weeks of the> maintenance phase are shown.
IMP: Investigational medicinal product, PYE: Patient years of exposure, N: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of adverse events, R: Rate (number of adverse events divided by patient years of exposure multiplied by 100).
1) Considered possibly or probably related to IMP by the investigator.

Shell 61: Overall summary of adverse events during <XXX> by randomised treatment and rescue medication: safety analysis set

	LEO 90100 remission (n=xxx)			Vehicle remission (n=xxx)			LEO 90100 relapse (n=xxx)			Vehicle relapse (n=xxx)		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
PYE	xxx.xx			xxx.xx			xxx.xx			xxx.xx		
Events	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Serious	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Severity												
Mild	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Moderate	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Severe	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Related[1] to IMP	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Leading to withdrawal from trial	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Action taken with IMP												
Dose not changed	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Drug withdrawn	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Not applicable	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Unknown	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Outcome												
Fatal	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Not recovered/Not resolved	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Recovering/Resolving	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x

continued...

	LEO 90100 remission (n=xxx)			**Vehicle remission (n=xxx)**			**LEO 90100 relapse (n=xxx)**			**Vehicle relapse (n=xxx)**		
	N (%)	**E**	**R**	**N (%)**	**E**	**R**	**N (%)**	**E**	**R**	**N (%)**	**E**	**R**
Recovered/Resolved	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Recovered/Resolved with sequelae	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Unknown	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x

AEs collected during the exposure time in the <total/first 28 weeks of the/remaining 24 weeks of the> maintenance phase are shown.
IMP: Investigational medicinal product, PYE: Patient years of exposure, N: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of adverse events, R: Rate (number of adverse events divided by patient years of exposure multiplied by 100).
1) Considered possibly or probably related to IMP by the investigator.

Shell 62: <XXX> during the open-label phase by SOC and preferred term: open-label safety analysis set

System Organ Class (SOC) Preferred term	Open-label LEO 90100 (n=xxx) N	(%)	E	R
PYE	xxx.x			
All AEs	xxx	(xx.x)	xxx	xxx.xx
SOC 1	xxx	(xx.x)	xxx	xxx.xx
Preferred term 1	xxx	(xx.x)	xxx	xxx.xx
...	xxx	(xx.x)	xxx	xxx.xx
Preferred term k_1	xxx	(xx.x)	xxx	xxx.xx
SOC 2	xxx	(xx.x)	xxx	xxx.xx
Preferred term 1	xxx	(xx.x)	xxx	xxx.xx
...	xxx	(xx.x)	xxx	xxx.xx
Preferred term k_2	xxx	(xx.x)	xxx	xxx.xx
...				
SOC M	xxx	(xx.x)	xxx	xxx.xx
Preferred term 1	xxx	(xx.x)	xxx	xxx.xx
...	xxx	(xx.x)	xxx	xxx.xx
Preferred term k_M	xxx	(xx.x)	xxx	xxx.xx

AEs collected during the exposure time in the initial open-label phase are shown. Classification according to MedDRA xx.x. N: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of adverse events, R: Rate (number of adverse events divided by patient years of exposure multiplied by 100).

Shell 63: <XXX> during <XXX> by SOC, preferred term, and randomised treatment: safety analysis set

System Organ Class (SOC) Preferred term	LEO 90100 (n=xxx)				Vehicle (n=xxx)			
	N	(%)	E	R	N	(%)	E	R
PYE	xxx.x				xxx.x			
All AEs	xxx	(xx.x)	xxx	xxx.xx	xxx	(xx.x)	xxx	xxx.xx
SOC 1	xxx	(xx.x)	xxx	xxx.xx	xxx	(xx.x)	xxx	xxx.xx
Preferred term 1	xxx	(xx.x)	xxx	xxx.xx	xxx	(xx.x)	xxx	xxx.xx
...	xxx	(xx.x)	xxx	xxx.xx	xxx	(xx.x)	xxx	xxx.xx
Preferred term k_1	xxx	(xx.x)	xxx	xxx.xx	xxx	(xx.x)	xxx	xxx.xx
SOC 2	xxx	(xx.x)	xxx	xxx.xx	xxx	(xx.x)	xxx	xxx.xx
Preferred term 1	xxx	(xx.x)	xxx	xxx.xx	xxx	(xx.x)	xxx	xxx.xx
...	xxx	(xx.x)	xxx	xxx.xx	xxx	(xx.x)	xxx	xxx.xx
Preferred term k_2	xxx	(xx.x)	xxx	xxx.xx	xxx	(xx.x)	xxx	xxx.xx
...								
SOC M	xxx	(xx.x)	xxx	xxx.xx	xxx	(xx.x)	xxx	xxx.xx
Preferred term 1	xxx	(xx.x)	xxx	xxx.xx	xxx	(xx.x)	xxx	xxx.xx
...	xxx	(xx.x)	xxx	xxx.xx	xxx	(xx.x)	xxx	xxx.xx
Preferred term k_M	xxx	(xx.x)	xxx	xxx.xx	xxx	(xx.x)	xxx	xxx.xx

AEs collected during the exposure time in the <total/first 28 weeks of the/remaining 24 weeks of the> maintenance phase are shown.
Classification according to MedDRA xx.x.
N: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of adverse events,
R: Rate (number of adverse events divided by patient years of exposure multiplied by 100).

Shell 64: <XXX> during <XXX> by SOC, preferred term, randomised treatment, and rescue medication: safety analysis set

	LEO 90100 remission (n=xxx)			Vehicle remission (n=xxx)			LEO 90100 relapse (n=xxx)			Vehicle relapse (n=xxx)		
System Organ Class (SOC) **Preferred term**	**N (%)**	**E**	**R**	**N (%)**	**E**	**R**	**N (%)**	**E**	**R**	**N (%)**	**E**	**R**
PYE	xxx.x			xxx.x			xxx.x			xxx.x		
All AEs	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
SOC 1	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Preferred term 1	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
...	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Preferred term k_1	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
SOC 2	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Preferred term 1	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
...	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Preferred term k_2	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
...												
SOC M	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Preferred term 1	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
...	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x
Preferred term k_M	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x	xxx(xx.x)	xxx	xxx.x

AEs collected during the exposure time in the <total/first 28 weeks of the/remaining 24 weeks of the> maintenance phase are shown. Classification according to MedDRA xx.x. N: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of adverse events, R: Rate (number of adverse events divided by patient years of exposure multiplied by 100).

Shell 65: Adverse events during the open-label phase by causal relationship to IMP, SOC, and preferred term: open-label safety analysis set

	Open-label LEO 90100 (n=xxx)		
System Organ Class (SOC) **Preferred term**	**NR** **E**	**PO** **E**	**PR** **E**
PYE	xxx.x		
All AEs	xxx	xxx	xxx
SOC 1	xxx	xxx	xxx
Preferred term 1	xxx	xxx	xxx
...	xxx	xxx	xxx
Preferred term k_1	xxx	xxx	xxx
...			
SOC M	xxx	xxx	xxx
Preferred term 1	xxx	xxx	xxx
...	xxx	xxx	xxx
Preferred term k_M	xxx	xxx	xxx

AEs collected during the exposure time in the initial open-label phase are shown.
Classification according to MedDRA xx.x. E: Number of adverse events, NR: Not Related, PO: Possibly Related, PR: Probably Related.

Shell 66: Adverse events during <XXX> by causal relationship to IMP, SOC, preferred term, and randomised treatment: safety analysis set

	LEO 90100 (n=xxx)			Vehicle (n=xxx)		
System Organ Class (SOC) **Preferred term**	**NR** **E**	**PO** **E**	**PR** **E**	**NR** **E**	**PO** **E**	**PR** **E**
PYE	xxx.x			xxx.x		
All AEs	xxx	xxx	xxx	xxx	xxx	xxx
SOC 1	xxx	xxx	xxx	xxx	xxx	xxx
Preferred term 1	xxx	xxx	xxx	xxx	xxx	xxx
...	xxx	xxx	xxx	xxx	xxx	xxx
Preferred term k_1	xxx	xxx	xxx	xxx	xxx	xxx
...						
SOC M	xxx	xxx	xxx	xxx	xxx	xxx
Preferred term 1	xxx	xxx	xxx	xxx	xxx	xxx
...	xxx	xxx	xxx	xxx	xxx	xxx
Preferred term k_M	xxx	xxx	xxx	xxx	xxx	xxx

AEs collected during the exposure time in the <total/first 28 weeks of the/remaining 24 weeks of the> maintenance phase are shown.
Classification according to MedDRA xx.x. E: Number of adverse events, NR: Not Related, PO: Possibly Related, PR: Probably Related.

Shell 67: Adverse events during <XXX> by causal relationship to IMP, SOC, preferred term, randomised treatment, and rescue medication: safety analysis set

	LEO 90100 remission (n=xxx)			Vehicle remission (n=xxx)			LEO 90100 relapse (n=xxx)			Vehicle relapse (n=xxx)		
System Organ Class (SOC) **Preferred term**	**NR** **E**	**PO** **E**	**PR** **E**	**NR** **E**	**PO** **E**	**PR** **E**	**NR** **E**	**PO** **E**	**PR** **E**	**NR** **E**	**PO** **E**	**PR** **E**
PYE	xxx.x			xxx.x			xxx.x			xxx.x		
All AEs	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
SOC 1	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Preferred term 1	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
...	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Preferred term k_1	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
...												
SOC M	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Preferred term 1	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
...	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Preferred term k_M	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

AEs collected during the exposure time in the <total/first 28 weeks of the/remaining 24 weeks of the> maintenance phase are shown.
Classification according to MedDRA xx.x. E: Number of adverse events, NR: Not Related, PO: Possibly Related, PR: Probably Related.

Shell 68: Physician's assessment of local safety and tolerability by visit in open-label phase: open-label safety analysis set

Physician's assessment of local safety and tolerability Visit	Open-label safety analysis set (n=xxx)	Randomised subjects (n=xxx)	Not randomised subjects (n=xxx)
Perilesional erythema			
Visit 1			
Number of subjects	xxx	xxx	xxx
Absent	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Visit 2			
<as above>			
Perilesional oedema			
<as above>			
Perilesional dryness			
<as above>			
Perilesional erosion			
<as above>			

Shell 69: Shift table for physician's assessment of local safety and tolerability from start to end of open-label phase: open-label safety analysis set

	All subjects in open-label safety analysis set (n=xxx)				Randomised subjects (n=xxx)				Not randomised subjects (n=xxx)			
Visit	**Visit 2**				**Visit 2**				**Visit 2**			
Physician's assessment of local safety and tolerability	**Absent**	**Mild**	**Mod**	**Sev**	**Absent**	**Mild**	**Mod**	**Sev**	**Absent**	**Mild**	**Mod**	**Sev**
Visit 1												
Perilesional erythema												
Absent	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Perilesional oedema												
<as above>												
Perilesional dryness												
<as above>												
Perilesional erosion												
<as above>												

Mod: Moderate, Sev: Severe

Shell 70: Physician's assessment of local safety and tolerability by visit not related to relapse: safety analysis set

Physician's assessment of local safety and tolerability **Visit**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
Perilesional erytnema		
Visit 2		
Number of subjects	xxx	xxx
Absent	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
...		
Visit 15		
<as above>		
Perilesional oedema		
<as above>		
Perilesional dryness		
<as above>		
Perilesional erosion		
<as above>		

Shell 71: Physician's assessment of local safety and tolerability by visit for start of relapse: safety analysis set

Physician's assessment of local safety and tolerability **Visit**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
Perilesional erythema		
Visit 2-visit 3		
Number of subjects	xxx	xxx
Absent	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Visit 3		
<as above>		
Visit 3-visit 4		
<as above>		
...		
Visit 14-visit 15		
<as above>		
Total		
Number of relapses	xxx	xxx
Number of subjects	xxx	xxx
Absent	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Perilesional oedema		
<as above>		
Perilesional dryness		
<as above>		
Perilesional erosion		
<as above>		

Shell 72: Physician's assessment of local safety and tolerability by visit for end of relapse: safety analysis set

Physician's assessment of local safety and tolerability **Visit**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
Perilesional erythema		
Visit 3-visit 4		
Number of subjects	xxx	xxx
Absent	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Visit 4		
<as above>		
Visit 4-visit 5		
<as above>		
...		
Visit 15		
<as above>		
Visit 15-UNS[1]		
<as above>		
Total		
Number of relapses	xxx	xxx
Number of subjects	xxx	xxx
Absent	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Perilesional oedema		
<as above>		
Perilesional dryness		
<as above>		
Perilesional erosion		
<as above>		

1) Possible unscheduled visits (UNS) after Visit 15 in the maintenance phase.

Shell 73: Shift table for physician's assessment of local safety and tolerability from start of relapse to end of relapse by visit for start of relapse: safety analysis set

	LEO 90100 (n=xxx)				Vehicle (n=xxx)			
	End of relapse				End of relapse			
Physician's assessment of local safety and tolerability **Visit**	**Absent**	**Mild**	**Mod**	**Sev**	**Absent**	**Mild**	**Mod**	**Sev**
Perilesional erythema								
Visit 2-visit 3								
Absent	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Visit 3								
Absent	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Visit 3-visit 4								
Absent	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
...								

continued...

	LEO 90100 (n=xxx)				Vehicle (n=xxx)			
	End of relapse				End of relapse			
Physician's assessment of local safety and tolerability **Visit**	**Absent**	**Mild**	**Mod**	**Sev**	**Absent**	**Mild**	**Mod**	**Sev**
Visit 14-visit 15								
Absent	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Total								
Absent	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Perilesional oedema								
<as above>								
Perilesional dryness								
<as above>								
Perilesional erosion								
<as above>								

Mod: Moderate, Sev: Severe

Shell 74: Subject's assessment of local safety and tolerability by visit in open-label phase: open-label safety analysis set

Subject's assessment of local safety and tolerability Visit	All subjects in open-label safety analysis set (n=xxx)	Randomised subjects (n=xxx)	Not randomised subjects (n=xxx)
Application site burning or pain			
Visit 1			
Number of subjects	xxx	xxx	xxx
Absent	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Visit 2			
<as above>			

Shell 75: Shift table for subject's assessment of local safety and tolerability from start to end of open-label phase: open-label safety analysis set

Visit	All subjects in open-label safety analysis set (n=xxx)				Randomised subjects (n=xxx)				Not randomised subjects (n=xxx)			
Subject's assessment of local safety and tolerability	Visit 2				Visit 2				Visit 2			
	Absent	Mild	Mod	Sev	Absent	Mild	Mod	Sev	Absent	Mild	Mod	Sev
Visit 1												
Application site burning or pain												
Absent	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Mod: Moderate, Sev: Severe

Shell 76: Subject's assessment of local safety and tolerability by visit not related to relapse: safety analysis set

Subject's assessment of local safety and tolerability Visit	LEO 90100 (n=xxx)	Vehicle (n=xxx)
Application site burning or pain		
Visit 2		
Number of subjects	xxx	xxx
Absent	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
...		
Visit 15		
<as above>		

Shell 77: Subject's assessment of local safety and tolerability by visit for start of relapse: safety analysis set

Subject's assessment of local safety and tolerability **Visit**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
Application site burning or pain		
Visit 2-visit 3		
Number of subjects	xxx	xxx
Absent	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Visit 3		
<as above>		
Visit 3-4		
<as above>		
Visit 4		
<as above>		
...		
Visit 14-visit 15		
<as above>		
Total		
Number of relapses	xxx	xxx
Number of subjects	xxx	xxx
Absent	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)

Shell 78: Subject's assessment of local safety and tolerability by visit for end of relapse: safety analysis set

Subject's assessment of local safety and tolerability **Visit**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
Application site burning or pain		
Visit 3-visit 4		
Number of subjects	xxx	xxx
Absent	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)
Visit 4		
<as above>		
Visit 4-5		
<as above>		
...		
Visit 15		
<as above>		
Visit 15-UNS[1]		
<as above>		
Total		
Number of relapses	xxx	xxx
Number of subjects	xxx	xxx
Absent	xxx (xx.x%)	xxx (xx.x%)
Mild	xxx (xx.x%)	xxx (xx.x%)
Moderate	xxx (xx.x%)	xxx (xx.x%)
Severe	xxx (xx.x%)	xxx (xx.x%)

1) Possible unscheduled visits (UNS) after visit 15 in the maintenance phase.

Shell 79; Shift table for subject's assessment of local safety and tolerability from start of relapse to end of relapse by visit for start of relapse: safety analysis set

Subject's assessment of local safety and tolerability	LEO 90100 (n=xxx)				Vehicle (n=xxx)			
	End of relapse				End of relapse			
Visit	Absent	Mild	Mod	Sev	Absent	Mild	Mod	Sev
Application site burning or pain								
Visit 2-visit 3								
Absent	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Visit 3								
Absent	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Visit 3-visit 4								
Absent								
Mild								
Moderate								
Severe								
...								
Visit 14-visit 15								
Absent	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

continued...

Subject's assessment of local safety and tolerability	LEO 90100 (n=xxx)				Vehicle (n=xxx)			
	End of relapse				End of relapse			
Visit	Absent	Mild	Mod	Sev	Absent	Mild	Mod	Sev
Total								
Absent	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Mild	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Moderate	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Severe	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Mod: Moderate, Sev: Severe

Shell 80: Change in vital signs from baseline to end of open-label phase: open-label safety analysis set

Vital sign **Change**	**Open-label LEO 90100** **(n=xxx)**
Parameter 1 (<unit>)	
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x
Parameter 2 (<unit>)	
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x
...	
Parameter k (<unit>)	
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile.

Shell 81: Change in vital signs from randomisation to end of maintenance phase <for subjects XXX>: safety analysis set

Vital sign **Change**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
<Parameter 1> (<unit>)		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
<Parameter 2> (<unit>)		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
...		
<Parameter k> (<unit>)		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile.

Shell 82: Change in laboratory parameters from baseline to end of open-label phase: open-label safety analysis set

Laboratory assessment **Laboratory parameter** **Change**	**Open-label LEO 90100** **(n=xxx)**
Biochemistry	
<Parameter 1> (<unit>)	
Number of subjects	xxx
Mean(SD)	x.xx(x.xx)
Median	x.xx
Q1;Q3	x.xx;x.xx
Min;Max	x.xx;x.xx
<Parameter 2> (<unit>)	
Number of subjects	xxx
Mean(SD)	x.xx(x.xx)
Median	x.xx
Q1;Q3	x.xx;x.xx
Min;Max	x.xx;x.xx
...	
Urinalysis	
<Parameter 1> (<unit>)	
Number of subjects	xxx
Mean(SD)	x.xx(x.xx)
Median	x.xx
Q1;Q3	x.xx;x.xx
Min;Max	x.xx;x.xx
<Parameter 2> (<unit>)	
Number of subjects	xxx
Mean(SD)	x.xx(x.xx)
Median	x.xx
Q1;Q3	x.xx;x.xx
Min;Max	x.xx;x.xx
...	

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile.

Shell 83: Change in laboratory parameters from randomisation to end of maintenance phase <for subjects XXX>: safety analysis set

Laboratory assessment **Laboratory parameter** **Change**	**LEO 90100** **(n=xxx)**	**Vehicle** **(n=xxx)**
Biochemistry		
<Parameter 1> (<unit>)		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
<Parameter 2> (<unit>)		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
...		
Urinalysis		
<Parameter 1> (<unit>)		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
<Parameter 2> (<unit>)		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
...		

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile.

Shell 84: Shift table for laboratory parameter categories at baseline against end of open-label phase: open-label safety analysis set

	Open-label LEO 90100 (n=xxx) End of open-label phase			
Laboratory assessment **Laboratory parameter**	**Low**	**Normal**	**High**	**Missing**
Biochemistry				
<Parameter 1>	xx	xx	xx	xx
Baseline Low	xx	xx	xx	xx
Baseline Normal	xx	xx	xx	xx
Baseline High	xx	xx	xx	xx
Baseline Missing				
<Parameter 2>				
...				
Urinalysis				
<Parameter 1>	xx	xx	xx	xx
Baseline Low	xx	xx	xx	xx
Baseline Normal	xx	xx	xx	xx
Baseline High	xx	xx	xx	xx
Baseline Missing				
<Parameter 2>				
...				

Shell 85: Shift table for laboratory parameter categories at randomisation against end of maintenance phase <for subjects XXX>: safety analysis set

	LEO 90100 (n=xxx)				Vehicle (n=xxx)			
	End of maintenance phase				End of maintenance phase			
Laboratory assessment Laboratory parameter	Low	Normal	High	Missing	Low	Normal	High	Missing
Biochemistry								
<Parameter 1>								
Randomisation Low	xx	xx	xx	xx	xx	xx	xx	xx
Randomisation Normal	xx	xx	xx	xx	xx	xx	xx	xx
Randomisation High	xx	xx	xx	xx	xx	xx	xx	xx
Randomisation Missing	xx	xx	xx	xx	xx	xx	xx	xx
<Parameter 2>								
...								
Urinalysis								
<Parameter 1>								
Randomisation Low	xx	xx	xx	xx	xx	xx	xx	xx
Randomisation Normal	xx	xx	xx	xx	xx	xx	xx	xx
Randomisation High	xx	xx	xx	xx	xx	xx	xx	xx
Randomisation Missing	xx	xx	xx	xx	xx	xx	xx	xx
<Parameter 2>								
...								

Shell 86: Compliance with treatment instructions during open-label treatment phase: open-label safety analysis

	Open-label LEO 90100 (n=xxx)
Number of subjects in non-compliance with treatment instructions	xxx(xx.x)
Number of daily IMP applications missed	xxx(xx.x)
Percentage of missed daily IMP applications:	
>0% and <=10%	xx(xx.x)
>10% and <=20%	xx(xx.x)
>20% and <=30%	xx(xx.x)
>30%	xx(xx.x)

Shell 87: Compliance with treatment instructions during maintenance phase excluding periods of treatment with rescue medication: maintenance phase safety analysis set

	LEO 90100 (n=xxx)	**Vehicle (n=xxx)**
Total maintenance phase		
Number of subjects in non-compliance with treatment instructions	xxx(xx.x)	xxx(xx.x)
Percentage of weeks in non-compliance with treatment instructions:		
>0% and <=10%	xx(xx.x)	xx(xx.x)
>10% and <=20%	xx(xx.x)	xx(xx.x)
>20% and <=30%	xx(xx.x)	xx(xx.x)
>30%	xx(xx.x)	xx(xx.x)
Visit 2 - visit 3		
Number of subjects	xxx	xxx
Number of subjects in non-compliance with treatment instructions	xxx(xx.x)	xxx(xx.x)
...		
Visit 14 - visit 15		
Number of subjects	xxx	xxx
Number of subjects in non-compliance with treatment instructions	xxx(xx.x)	xxx(xx.x)

Shell 88: Compliance with treatment instructions during periods of treatment with rescue medication: maintenance phase safety analysis set

	LEO 90100 (n=xxx)	**Vehicle (n=xxx)**
No of daily IMP applications missed	xx(xx.x)	xx(xx.x)
Percentage of missed daily IMP applications:		
>0% and <=10%	xx(xx.x)	xx(xx.x)
>10% and <=20%	xx(xx.x)	xx(xx.x)
>20% and <=30%	xx(xx.x)	xx(xx.x)
>30%	xx(xx.x)	xx(xx.x)

Shell 89: Duration of exposure during the open-label treatment phase: open-label safety analysis set

	Open-label LEO 90100 (n=xxx)
Duration of exposure	
Number of days	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile.

Shell 90: Duration of exposure during the maintenance phase: safety analysis set

	LEO 90100 (n=xxx)	**Vehicle (n=xxx)**
Duration of exposure		
Number of days	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile.

Shell 91: Amount of investigational medicinal product used during open-label treatment phase: open-label safety analysis set

Amount of IMP used	**Open-label LEO 90100 (n=xxx)**
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile.
The amount of IMP used is normalised by the number of days in the open-label phase for each subject.

Shell 92: Amount of investigational medicinal product used during maintenance phase: safety analysis set

	LEO 90100 (n=xxx)		Vehicle (n=xxx)	
	Total IMP	**Rescue IMP**	**Total IMP**	**Rescue IMP**
Number of subjects	xxx	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile.
The amount of IMP used for each subject is normalised by the number of days in the maintenance phase or number of days in remission, respectively.

Shell 93: Cumulative amount of investigational medical product used up to scheduled visits: maintenance phase safety analysis set

	LEO 90100 (n=xxx)	Vehicle (n=xxx)
Visit 3		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
...		
Visit 15		
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x

SD: Standard deviation, Q1: 1st quartile, Q3: 3rd quartile.

Shell 94: Serum-cortisol concentration at time 0 and at 30 and at 60 minutes after ACTH-challenge test by visit: open-label HPA analysis set

	Open-label LEO 90100 (n=xxx)
Visit 1	
0 min (before ACTH-challenge test)	
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x
30 min after ACTH-challenge test	
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x
60 min after ACTH-challenge test	
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x
Visit 2	
0 min (before ACTH-challenge test)	
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x
30 min after ACTH-challenge test	
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x
60 min after ACTH-challenge test	
Number of subjects	xxx
Mean(SD)	xx.x(xx.x)
Median	xx.x
Q1;Q3	xx.x;xx.x
Min;Max	xx.x;xx.x

Shell 95: Individual data for subjects with serum cortisol concentration ≤18 mcg/dL at either 30 minutes or 60 minutes after ACTH-challenge: open-label HPA analysis set.

Subject	Visit	Sample time	Serum cortisol concentration (mcg/dL)	Change in serum cortisol concentration from time 0 (mcg/dL)	BSA (%)
<subject id>	Visit xx	0 min	xx.x		xx.x
		30 min	xx.x	xx.x	
		60 min	xx.x	xx.x	
	Visit xx	0 min	xx.x		xx.x
		30 min	xx.x	xx.x	
		60 min	xx.x	xx.x	
	...				
<subject id>	Visit xx	0 min	xx.x		xx.x
		30 min	xx.x	xx.x	
		60 min	xx.x	xx.x	
	Visit xx	0 min	xx.x		xx.x
		30 min	xx.x	xx.x	
		60 min	xx.x	xx.x	
...					

Shell 96: Subjects with serum cortisol concentration ≤18 mcg/dL at both 30 and 60 minutes after ACTH-challenge in open-label phase; open-label HPA analysis set

Visit Serum Cortisol Concentration (mcg/dL)	Open-label LEO 90100 (n=xxx) Number of subjects (%)
Visit 1	
30 min after ACTH challenge test	
≤18 mcg/dL	xx(xx.x)
>18 mcg/dL	xx(xx.x)
Total	xx(xx.x)
60 min after ACTH challenge test	
≤18 mcg/dL	xx(xx.x)
>18 mcg/dL	xx(xx.x)
Total	xx(xx.x)
30 and 60 min after ACTH challenge test	
≤18 mcg/dL	xx(xx.x)
>18 mcg/dL	xx(xx.x)
Total	xx(xx.x)
Visit 2	
30 min after ACTH challenge test	
≤18 mcg/dL	xx(xx.x)
>18 mcg/dL	xx(xx.x)
Total	xx(xx.x)
60 min after ACTH challenge test	
≤18 mcg/dL	xx(xx.x)
>18 mcg/dL	xx(xx.x)
Total	xx(xx.x)
30 and 60 min after ACTH challenge test	
≤18 mcg/dL	xx(xx.x)
>18 mcg/dL	xx(xx.x)
Total	xx(xx.x)

Shell 97: Serum-cortisol concentration at time 0 and at 30 and at 60 minutes after ACTH-challenge test by visit: HPA analysis set

	All randomised subjects in the HPA axis group (n=xxx)	**LEO 90100 (n=xxx)**	**Vehicle (n=xxx)**
Visit 2			
0 min (before ACTH-challenge test)			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
30 min after ACTH-challenge test			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median-	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
60 min after ACTH-challenge test			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Visit 8			
0 min (before ACTH-challenge test)			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
30 min after ACTH-challenge test			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
60 min after ACTH-challenge test			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x

continued…

	All randomised subjects in the HPA axis group (n=xxx)	**LEO 90100 (n=xxx)**	**Vehicle (n=xxx)**
Visit 15			
0 min (before ACTH-challenge test)			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
30 min after ACTH-challenge test			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
60 min after ACTH-challenge test			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x

Shell 98: Subjects with serum cortisol concentration ≤18 mcg/dL at both 30 and 60 minutes after ACTH-challenge in maintenance phase; HPA analysis set

Visit Serum Cortisol Concentration (mcg/dL)	All randomised subjects in the HPA axis group (n=xxx) Number of subjects (%)	LEO 90100 (n=xxx) Number of subjects (%)	Vehicle (n=xxx) Number of subjects (%)
Visit 2			
30 min after ACTH challenge test			
≤18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
>18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
Total	xx(xx.x)	xx(xx.x)	xx(xx.x)
60 min after ACTH challenge test			
≤18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
>18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
Total	xx(xx.x)	xx(xx.x)	xx(xx.x)
30 and 60 min after ACTH challenge test			
≤18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
>18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
Total	xx(xx.x)	xx(xx.x)	xx(xx.x)
Visit 8			
30 min after ACTH challenge test			
≤18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
>18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
Total	xx(xx.x)	xx(xx.x)	xx(xx.x)
60 min after ACTH challenge test			
≤18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
>18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
Total	xx(xx.x)	xx(xx.x)	xx(xx.x)
30 and 60 min after ACTH challenge test			
≤18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
>18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
Total	xx(xx.x)	xx(xx.x)	xx(xx.x)

continued…

Visit Serum Cortisol Concentration (mcg/dL)	All randomised subjects in the HPA axis group (n=xxx) Number of subjects (%)	LEO 90100 (n=xxx) Number of subjects (%)	Vehicle (n=xxx) Number of subjects (%)
Visit 15			
30 min after ACTH challenge test			
≤18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
>18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
Total	xx(xx.x)	xx(xx.x)	xx(xx.x)
60 min after ACTH challenge test			
≤18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
>18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
Total	xx(xx.x)	xx(xx.x)	xx(xx.x)
30 and 60 min after ACTH challenge test			
≤18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
>18 mcg/dL	xx(xx.x)	xx(xx.x)	xx(xx.x)
Total	xx(xx.x)	xx(xx.x)	xx(xx.x)

Shell 99: Individual data for subjects with serum cortisol concentration ≤18 mcg/dL at either 30 minutes or 60 minutes after ACTH-challenge: HPA analysis set.

Subject	Visit	Sample time	Serum cortisol concentration (mcg/dL)	Change in serum cortisol concentration from time 0 (mcg/dL)	BSA (%)
<subject id>	Visit xx	0 min	xx.x		xx.x
		30 min	xx.x	xx.x	
		60 min	xx.x	xx.x	
	Visit xx	0 min	xx.x		xx.x
		30 min	xx.x	xx.x	
		60 min	xx.x	xx.x	
	...				
<subject id>	Visit xx	0 min	xx.x		xx.x
		30 min	xx.x	xx.x	
		60 min	xx.x	xx.x	
	Visit xx	0 min	xx.x		xx.x
		30 min	xx.x	xx.x	
		60 min	xx.x	xx.x	
...					

Shell 100: Serum-cortisol concentration at time 0 and at 30 and at 60 minutes after ACTH-challenge in the follow-up phase: HPA analysis set

	All randomised subjects in the HPA axis group (n=xxx)	**LEO 90100 (n=xxx)**	**Vehicle (n=xxx)**
Follow-up visit 2			
0 min (before ACTH-challenge test)			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
30 min after ACTH-challenge test			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median-	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
60 min after ACTH-challenge test			
Number of subjects	xxx	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x	xx.x;xx.x

Shell 101: Summary of rebounds occurring within 2 months after discontinuing open-label phase treatment or relapse treatment: safety analysis set

	LEO 90100 (n=xxx)	Vehicle (n=xxx)
Within 2 months after discontinuation of open-label treatment:		
Number of rebounds	xxx	xxx
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x
Within 2 months after discontinuation of relapse treatment:		
Number of rebounds	xxx	xxx
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x

Shell 102: Summary of rebounds occurring within 2 months after discontinuing of maintenance treatment: safety analysis set

	LEO 90100 (n=xxx)	Vehicle (n=xxx)
Within 2 months after discontinuation of maintenance treatment:		
Number of rebounds	xxx	xxx
Number of subjects	xxx	xxx
Mean(SD)	xx.x(xx.x)	xx.x(xx.x)
Median	xx.x	xx.x
Q1;Q3	xx.x;xx.x	xx.x;xx.x
Min;Max	xx.x;xx.x	xx.x;xx.x

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